IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Christoph Ruedinger et al.

Serial No.: 10/595,174

Filed: March 17, 2006

For: METHOD FOR THE PRODUCTION OF ISOCYANATOORGANOSILANES

Group Art Unit: 1621

Examiner: Jennifer Y. Cho

Attorney Docket No.: WAS 0742 PUSA

APPEAL BRIEF UNDER 37 C.F.R. § 41.37

Mail Stop Appeal Brief - Patents
Commissioner for Patents
U.S. Patent & Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is an Appeal Brief from the final rejection of claims 16 - 31 of the Office Action mailed on May 22, 2008 for the above-identified patent application.

I. REAL PARTY IN INTEREST

The real party in interest is Wacker Chemie AG ("Assignee"), a corporation organized and existing under the laws of Germany, and having a place of business at Hanns-Seidel-Platz 4, 81737 München, Germany, as set forth in the assignment recorded in the U.S. Patent and Trademark Office on May 21, 2007, at Reel 019728/Frame 0028.

II. RELATED APPEALS AND INTERFERENCES

There are no appeals, interferences or judicial proceedings known to the Appellant, the Appellants' legal representative, or the Assignee which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF CLAIMS

Claims 16 - 31 are pending in this application. Claims 16 - 31 have been rejected and are the subject of this appeal. Claims 1 - 15 have been cancelled.

IV. STATUS OF AMENDMENTS

An amendment after final rejection was filed on August 22, 2008, and has been denied entry, even though no claim amendments were made.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The claimed invention is a process for preparing isocyanatoorganosilanes by thermolysis of carbamatoorganosilanes, wherein the thermolysis takes place by exposure to microwave radiation. Claim 1 as filed; disclosure page 1 lines 3 - 4; page 2, lines 21 - 24.

Claim 19 requires the thermolysis to take place in the absence of a catalyst. Disclosure page 4, lines 15 - 19; pages 10 - 11, Example 1.

Claim 20 requires a homogenous catalyst to be used. Claims 4 and 5 as filed; page 4, lines 15 - 30.

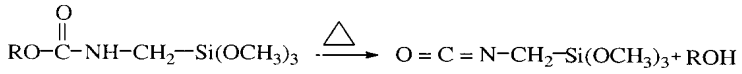
Claim 31 requires a gas-phase reactor containing a heterogenous catalyst to be located downstream from the microwave reaction chamber. Claim 15 as filed; disclosure page 9, lines 26 - 31.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Claims 16 - 31 stand rejected under 36 U.S.C. § 103(a) as unpatentable over Kammel et al. U.S. 6,812,361 ("*Kammel*") in view of Greene et al. U.S. 6,084,226 ("*Greene*").

VII. ARGUMENT

The claimed subject matter is directed to the synthesis of isocyanatoorganosilanes by thermolytic cleavage of carbamatoorganosilanes. The reaction may be illustrated by the preparation of isocyanatomethyltrimethoxysilane:



The reaction *per se* is old. For example, alkylene diisocyanates which are very useful in UV-resistant polyurethane elastomers and coatings are difficult to prepare by conventional phosgenation of alkylene diamines. Moreover, this synthetic method employs the very toxic gaseous phosgene, which was once used in gas warfare. Thus, in the 1980's, researchers such as *Merger* and *Towae* attempted to prepare such isocyanates by the thermolysis of bis(carbamato)alkanes, formed by the reaction between diamines, urea, and alcohol. However, the process is a complicated one, since the thermolysis liberates alcohols which are exothermically reactive with the product isocyanate, thus requiring complicated separation of these reactive cleavage products. Moreover, the isocyanate group is so reactive that it may react with itself to form carbodiimides (dimers) and isocyanurates (trimers), and with carbamates to form numerous other compounds such as polyureas as well. Such byproducts, especially the isocyanurates and polyureas, clog the apparatus.

The formation of oligomers and other byproducts has always been a problem with carbamate thermolysis. However, because of the difficulties of preparing isocyanatoorganosilanes by other methods, thermolytic processes have been investigated over the years despite the drawbacks of thermolysis. For example, Berger U.S. 3,598,852 ("*Berger*") discloses thermolysis of methylcarbamatopropyltrimethoxysilane at 160°C at 1 mm pressure. The reaction of only 119 g of carbamate took five hours(!) and gave a 73% yield of product. Such a long reaction is very economically undesirable, and the process produces solid byproducts

(isocyanurates) which ultimately clog the reaction vessel and distillation column, making continuous operation impossible.

This liquid phase reaction is discussed by Sheridan et al. U.S. 6,008,396 ("*Sheridan*") who indicates that such liquid phase reactions are unacceptable:

> All liquid phase processes disclosed thus far[1] suffer from one or more disadvantages of low yield, slow kinetics, need for highly toxic raw materials, need for extensive work-up or purification, often in the presence of higher levels of close-boiling contaminants, and substantial generation of by-products and waste materials.

Sheridan, column 1, lines 23 - 28.

Sheridan proposed to improve isocyanatoorganosilane synthesis by slowly metering the starting carbamate into very hot liquid at low pressure. Liquids used included, *inter alia,* paraffinic oils and polydimethylsiloxanes. *Sheridan* compares his method with that of *Berger* in his comparison example in column 6. A yield of 67.3% (slightly less than that achieved by *Berger* - 73%) was obtained in the liquid phase process, but "heavies" (byproducts) remained in the reactor in an amount of 28% relative to starting carbamate.

EP 0 649 850 A1 ("*Mui*") also attests to the problems associated with liquid phase thermolysis, as well as citing the continuing need for an economical method of preparing isocyanatoorganosilanes. *See, e.g.* page 2, lines 8 - 11. At page 2, lines 17 - 20, *Mui* echoes the sentiments of *Sheridan* relative to liquid phase processes:

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[1]*Sheridan* was filed (provisional) on April 11, 1997, and cites Berger U.S. 3,598,852 (liquid phase process).

> All liquid phase processes disclosed thus far suffer from one or more disadvantages of low yield, slow kinetics, need for highly toxic raw materials, need for extensive work-up or purification, often in the presence of higher levels of close-boiling contaminants, and substantial generation of by-products and waste materials.

To overcome these obstacles, *Mui* proposed a vapor phase pyrolysis of carbamatoorganosilanes, and thus teaches against liquid phase processes.

Kammel (commonly assigned), was published as U.S. 2004/0049064 on March 11, 2004, and issued as U.S. Patent 6,812,361 B2 on November 2, 2004. Both these dates are after Appellants' German priority date of December 11, 2003, and thus *Kammel* is only a reference under 35 U.S.C. § 102(e). Since *Kammel* is commonly assigned, and subject to an obligation of common assignment at the time the claimed invention was made, *Kammel* is not believed to be a proper reference under 35 U.S.C. § 103(c). However, to avoid reopening prosecution, Appellants note to the Board that the *Kammel* PCT application, of which U.S. 6,812,361 is a National Phase thereof, was published on June 27, 2002, and the published PCT is thus prior art. Appellants agree to substitute this application, which was published in the German language, for Kammel U.S. 6,812,361, but will continue to refer to the latter rather than the German language PCT application.

Kammel also stresses the continuing need for economical processes for producing isocyanatoorganosilanes. *See, e.g. Kammel* at column 1, lines 11 - 17. *Kammel* discusses the process of *Sheridan* at column 1, lines 24 - 30, but indicates that in the *Sheridan* process, there is a continual build-up of byproducts which in a very short time significantly decreases the purity of the product, as indicated by *Sheridan* himself at column 6, lines 41 - 49.

Kammel also discusses the liquid phase process, referring to EP-A-1010704. In the latter, the starting carbamates are produced by reacting aminoorganosilane with urea and

alcohol, in similar fashion to *Merger* and *Towae*. The purified carbamatoorganosilane thus obtained is then thermolyzed in the liquid phase as was done by *Berger*. *Kammel* notes that the liquid phase process (despite having been patented by *Berger* in 1971(!!)) had not been used industrially as of *Kammel's* filing date in 2001, some 30 years later after *Berger* issued. Thus, *Kammel*, like *Sheridan* and *Mui*, teaches avoiding liquid phase processes.

Kammel also discusses the gas phase thermolysis of EP-A-649850 (*Mui*, previously discussed). However, *Kammel* indicates that the yields of that gas phase process are unsatisfactory.

Kammel improved upon the prior art by a gas phase thermolysis in the presence of a heterogenous catalyst. By employing a solid catalyst and a gas phase reaction, byproducts are minimized and high product purity is obtained after simple distillation of the crude thermolysate. *See Kammel*, column 2, line 65 to column 3, line 2. In lines 1 and 2 of column 3, *Kammel* refers to the *caveat* of *Berger* that high thermal stress should be avoided, since this leads to increased formation of isocyanurate byproduct. Note *Berger* at lines 24 - 30, where he states that:

> Experience has shown that if the silylorganocarbamate is heated too rapidly. . .isocyanurate of the formula 3 can be formed along with the isocyanate of Formula 1. (emphasis added)

In the claimed invention, thermolysis takes place by heating the carbamatoorganosilane with microwaves in the liquid phase. By doing so, products of high purity (>97%) can be obtained by simple distillation, while the formation of isocyanurates at high thermal stress (as discussed by *Kammel* and *Berger*) is virtually eliminated. *See, e.g.* page 9, lines 19 - 25, and Examples 1 and 2.

1. The Claims Are Patentable Over *Kammel* and *Greene*

The claims have been rejected under 35 U.S.C. § 103(a) over *Kammel* in view of *Greene*. *Kammel* discloses a gas phase reaction with a heterogenous catalyst. *Greene* discloses the use of duty cycle-moderated microwaves to assist liquid phase reactions such as *Kjeldahl* digestions.

Kammel and *Greene* are not properly combinable. *Kammel* discloses a gas phase reaction. Microwaves are not absorbed by gases to any significant degree. This is so well known that Judicial Notice may be taken thereof. Microwaves heat liquids and some solids by increasing the rotational energy levels of molecules as they absorb this energy. If the molecules with higher rotational energy levels contact other molecules, their rotational energy may be transferred as kinetic energy, thus increasing the temperature. In the liquid phase, the molecules are free to move, and also abut each other, and thus provided the microwave frequency is in the range of rotational energy levels, efficient transfer of microwave energy into thermal energy results due to the huge number of rapidly occurring collisions. However, in many solids, molecules are restrained in position, rotational movement is not allowed, and therefore transfer of rotational energy is prohibited. Thus, for example, while liquid water is very rapidly heated by microwaves, ice is not. Ice is microwave transparent.

Likewise, while gas molecules may absorb microwave energy, and thus increase their rotational energy levels, the molecules in the gas phase are widely separated, and thus energy transfer from one molecule to another is a very rare event. Steam, for example, cannot be heated by microwaves.

That this is well known is supported by numerous treatises. One such treatise is C. Oliver Kappe, MICROWAVES IN ORGANIC AND MEDICINAL CHEMISTRY, Wiley-VCH, v. 25, p. 12, which was cited in Appellants' Amendment After Final. This amendment was not entered,

although *Kappe* was cited earlier in prosecution, and pages 3 and 4 of this reference are of record. However, *Kappe* is just one instance of numerous publications which indicate that microwaves do not heat gases.

Thus, there is no motivation to combine *Greene* with *Kammel*, since *Kammel* is a gas phase process and microwaves do not heat gases. The rejection should be reversed for this reason alone.[2]

Second, even were *Kammel* and *Greene* combinable, the combination does not teach or suggest the claimed invention. The claimed invention is a liquid phase process. While the term "liquid" does not appear in the claims *per se*, it is abundantly clear that this is the case. The claims require thermolysing by exposing the carbamatoorganosilane to microwaves. Since exposure of gases to microwaves does not result in any increase in temperature, it is clear and inherent that the carbamates are in the liquid phase. This is consistent with the entire specification. Claims must be read in view of the specification of which they are a part. *Markman v. Westview Instruments, Inc.*, 52 F. 3d 967, 969 (Fed. Cir.) aff'd. 517 US 370 (1996). *Kammel* teaches only a gas phase process, and severely criticizes liquid phase processes. Thus, *Kammel* teaches away from the claimed invention. The rejection should be reversed for this reason as well.

Third, the claimed process has produced surprising and unexpected results, as indicated by the Examples and Comparative Example.

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[2]Furthermore, there is no evidence of record which supports the proposed combination. As the Federal Circuit has stated, there must be clear and particular evidence of motivation to combine. *In re Dembiczak*, 175 F.3d 994, 50 USPQ 2d 1614 (Fed. Cir. 1999) and mere conclusory statements standing alone are not "evidence" *McElmurry v. Arkansas Power and Light*, 995 F.2d 1576, 27 USPQ 2d 1129 (Fed. Cir. 1993). Here, there is no evidence.

In Comparative Example 1, methylcarbamatopropyltrimethoxysilane ("MCPTS") was heated very rapidly (to minimize any effect of "time to temperature") to 225°C with a heterogenous Fe_2O_3 catalyst in a glass vessel with distillation column and overhead condenser. The sample size was also very small, which also reduced the heating time, such that the "time to temperature" was only a small fraction of the total reaction time. Even after 60 minutes at 225°C, no overhead condensate was collected, and analysis of the still residue revealed that 96% of the MCPTS remained unreacted (or had reacted and reverted). Only 0.9% of product, γ-isocyanatopropyltrimethoxysilane ("IPTS") was formed, along with 2.6% byproducts, both still contained in the reaction vessel. The ratio of byproduct to product was 2.9, in other words almost 300%!

Example 2 is directly comparable, employing exactly the same amounts of reactant and catalyst. After only 4 minutes, 1.7 ml of condensate from the refluxing mixture was obtained. The condensate contained 16% IPTS and 25% MCPTS, which could be recycled. The still bottoms contained 85% by weight unreacted MCPTS, 12.5% by weight of IPTS, and 2.5% byproducts. The ratio of byproducts to IPTS in the still was only 0.20. When the IPTS in the overhead is included also, the ratio even decreases slightly to about 0.19. These figures are less than 10% of the amount of byproducts formed in the purely thermal reaction. It was the large proportion of byproducts formed in liquid thermolysis which prevented the processes of *Berger* and *Sheridan* from being viable commercial processes. Appellants' process reduced byproduct formation by a factor of 10!

There is no way that the decrease in byproduct formation relative to product yield could have been predicted. The decrease in byproduct amount is dramatic, surprising, and unexpected. Further surprising and unexpected is that in the comparative example, despite being above the carbamate decomposition temperature for nearly 60 minutes, no overhead was collected. The industrial preparation of IPTS requires a continuous or semibatch technique. It is clearly impossible industrially to heat (by any means) a commercially sized batch of MCPTS

to form only a minuscule amount of product in the reaction vessel, and then isolate that minuscule amount by distillation from the remainder. The microwave assisted process not only produces higher yield and less byproduct, with a reaction rate some 75 times higher[3], but is also commercially viable.

There is absolutely no way to explain why the microwave assisted reaction produces a 75 times (7500%!!) greater yield than a purely thermal process, and in only 4 minutes as compared with one hour! Perhaps the uncatalyzed reaction is more instructive. This reaction showed a 40 times (4000%) increase in yield with microwaves as compared to the thermal reaction with catalyst. This is not a case, as in *KSR v. Teleflex*, 550 U.S. 398 (2007), where a combination of a limited number of alternatives achieved only the expected result. Here, there is no expected result.[4]

The Examiner has cited an "expected" result of a higher yield due to an increased heating rate which might be possible with microwaves. However, the Examples and Comparative Examples do not bear this out. The Comparative Example employed the same very small amount of reactant (20 ml) in a glass vessel in a very hot oil bath. Anyone who has had a laboratory course in organic chemistry knows that the reactant would reach the temperature of the oil bath within only a few minutes. However, no overhead was produced, even after one hour! By contrast, the subject invention microwave heated examples produced overhead after only 4 minutes. Even if the oil bath heated reactant were not to have reached 225°C after even a half hour, which is entirely unreasonable, what happened during the last 30 minutes? Why was no overhead obtained, since 225°C is above the boiling point of the reactant and far above the

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[3]Unlike comparing reactions in open v. closed pressurized vessels, Comparative Example 1 and Example 2 are directly comparable, since their maximum temperature is limited by the boiling point of the neat reactants, and both are performed at atomospheric pressure.

[4]With *Kammel*, this is especially true. There is no reason to believe that microwaves would have any effect on a gas phase reaction.

temperature at which it decomposes (*Berger* used only 160°C, for example, at a pressure of 1 mm Hg).

Thus, the "rapid heating" alleged by the Examiner cannot be a factor in generating increased yield and reaction rate. It also does not explain why the reaction should produce less byproduct. If the Examiner is correct in her assumption that microwaves somehow result in increased heating[5], then one would also expect increased byproduct production due to increased thermal stress, as indicated by *Berger* and *Kammel*. Thus, the fact that the claimed process produces less (considerably less) byproduct is not only highly unexpected, but completely unexplainable.

Moreover, there is no known relationship between yields obtained through microwave heating in comparison to thermal heating. This was fully explained in the Response of February 17, 2008, and is repeated below.

As indicated by Bernd Ondruschka, Letters, CHEMICAL AND ENGINEERING NEWS, March 28, 2005, the "optimism" for use of microwave assisted synthesis is not justified, citing recent investigations in Jena, Germany. G. Majetich et al., "The Use of Microwave Heating to Promote Organic Reactions," J. MICROWAVE POWER AND ELECTROMAGNETIC ENERGY, Vol. 30, 1, pp. 28 - 45 investigated a number of reactions including the reversible Diels-Alder Reaction, Cope and Claisen Rearrangements, ene reactions, conversion of alcohols to bromides, conversion of organic bromides to iodides, oxidations, and Fischer Esterifications. The results show that microwave synthesis generally reduced reaction time significantly, but did so because the microwave samples were conducted in sealed pressure containers, which allowed the reaction to take place at higher temperature, which is not possible under open reflux conditions. Thus, the duration of the reactions are not directly comparable, and cannot be used to assess reaction

[5]Which cannot be correct, since the limiting temperature of a liquid is its boiling point, no matter how much heat is applied.

rates, since the reactions took place at different temperatures. When corrected for this temperature differential (which was due to use of pressurized containers) by application of the Arrhenius equation, the ratio of reaction rates of all microwave assisted reaction to the thermal reaction varied widely, from only 10% of the reaction rate of the purely thermal reaction to 72 times the rate. In the 45 reactions studied, 22, or about 50%, were slower than the corresponding thermal reactions. There was absolutely no predictability in these results. For example, in the Diels-Alder Reactions (1-5), the relative ratios were 0.91, 6.0, 0.87, 0.54, and 0.10.

Moreover, the yields varied widely as well. In the Diels-Alder Reaction, the ratios of microwave yield to conventional thermal yield were 0.87, 1.26, 0.98, 0.91, and 1.04 - - in other words, in most reactions, a decrease in yield. In the ene reactions, three examples showed increases in yield, with yield ratios ranging from 2.35 to 1.10. In conversion of organic bromides to iodides, in the three examples, there was on average very little effect on yield. In the Fischer esterifications, on average the yields dropped when using microwaves. In aryl ether cleavage, all three reactions studied showed a very slight decrease in yield when microwaved. A study of the 45 examples clearly indicates to one skilled in the art, that provided the reaction can take place in a pressurized environment, reaction times can be considerably shortened due to the increased reaction temperature, but yield is very substrate dependent, and cannot be predicted. If conditions (pressure and temperature) are the same, however, as is the case in neat and solution reactions, even the relative rates are expected to be the same. The article also produces the conclusion that even when the rates are different, the actual reaction rates will only vary from about 0.5 (slower) to 2.0 for the vast majority of reactions.

C. Oliver Kappe et al., MICROWAVES IN ORGANIC AND MEDICINAL CHEMISTRY, Wiley-VCH ©2005 indicates on pages 3 - 4 that for solvent borne reactions, reflux temperature is a limiting factor, and for this reason, high boiling solvents have been used in open vessels, but present "serious challenges to product isolation and recycling of solvent." This reference may be viewed on the web.

Gedye and *Wei* investigated the synthesis of 1,5-diazepin-2-ones by thermal and microwave techniques, and found virtually no difference in rates or yields between the microwave and thermally heated reactions. *Gedye et al.*, CAN. J. CHEM., 1998, 76, 525-532.

It is clear from the foregoing references that there is no predictability with respect to "microwave assisted synthesis". For some classes of reactions, microwave usage results in lower yields generally, whereas in others, an improvement of yield occurs. But even within the same reaction class, some reactions will be slower and some faster. It is noted that when improved results are attained, they are generally due to higher temperatures as a result of using a closed vessel, the reason why pressure cookers were once quite popular.

To summarize, the references cited are not properly combinable; if combined, they do not teach or suggest the claimed invention; and there are no expected results obtained by Appellants' claimed process within the ambit of *KSR*, only unexpected results for which there is no explanation. The claimed invention is clearly non-obvious. Reversal of the rejection of claims 16 - 31 is solicited for the foregoing reasons.

2. Claim 19 is Separately Patentable

Claim 19 requires the reaction to be uncatalyzed. This is possible in the claimed invention because the reaction rate is so unexpectedly high when microwaves are used. Traces of thermolysis catalyst in the product can alter the storage stability and reactivity of the product, because the same catalysts which catalyze thermolysis also catalyze reactivity of the isocyanate group. Tin catalysts, for example are employed in numerous polyurethane systems as catalysts for isocyanate reactivity. Thus, eliminating catalysts, which also eliminates the potential for trace amounts to be included in the product, would be desirable.

Kammel teaches against uncatalyzed reactions. *Kammel* requires a heterogenous catalyst in his gas phase reaction. Teaching away is strong evidence of non-obviousness. *W.L. Gore v. Garlock*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983). Claim 19 is separately patentable, and reversal of the rejection of claim 19 is respectfully solicited for this additional reason.

3. Claim 20 is Separately Patentable

Claim 20 requires the use of a homogenous catalyst. Homogenous catalysts can only be used in liquid phase processes. Catalysts require contact with the substrates whose reaction they catalyze - they cannot "work at a distance." Anyone familiar with catalysis is aware of this. *Kammel* teaches a gas phase process. Homogenous catalysts cannot be used in such processes since collision of molecules in the gas phase with each other is very limited, as opposed to liquids, wherein the molecules abut each other.

Moreover, *Kammel* is very specific in requiring heterogenous catalysts. By requiring heterogenous catalysts, *Kammel* teaches away from homogenous catalysts. There is certainly no motivation for the skilled artisan to add a homogenous catalyst to a gas phase reaction of any kind, and *Kammel* teaches against doing so. Claim 20 is separately patentable. Reversal of the rejection of claim 20 is respectfully solicited.

4. Claim 31 is Separately Patentable

Claim 31 requires a gas phase reactor containing a heterogenous catalyst downstream from the microwave heated liquid phase reactor. *Kammel* does not teach or suggest such an arrangement, nor does *Greene*. There is no factual basis for this rejection, as was pointed out to the Office in Appellants' response of February 17, 2008. The Office replied that "this argument [is not]. . .persuasive, since the dependent claims are drawn to small modifications in

the claimed invention. . . . One skilled in the art usually makes fine adjustments and optimizes parameters."

This appears contrary to the concept of compact prosecution of the MPEP, and also fails as a matter of law. The use of a packed gas phase reactor following a microwave assisted reactor is clearly not simply a "small modification" or "fine adjustment". Rejections must be based on facts, not upon unsupported conclusions. *In re Soli*, 317 f.2d 941, 137 USPQ 797 (CCPA 1963); *In re Wagner*, 371 F.2d 877, 152 USPQ 552 (CCPA 1967).

Here, *Kammel* discloses that liquid phase reactions such as those of *Berger* are unsatisfactory, and purely gas phase reactions should be used instead. Thus, one skilled in the art would not be motivated to modify *Kammel* by prefacing his gas phase reaction with a liquid phase thermolysis of any type.

The rejection of claim 31 should be reversed, since there is no articulated ground of rejection, and since the principle reference *Kammel*[6] mitigates against the combination.

Reversal of all rejections of record is solicited.

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[6]It is noted that *Greene* adds nothing to *Kammel* as discussed with respect to the separate patentability of all of claims 19, 20, and 31.

The fee of $540.00 as applicable under the provisions of 37 C.F.R. § 41.20(b)(2) is being transmitted electronically herewith. Please charge any additional fees or credit any overpayments as a result of the filing of this paper to our Deposit Account No. 02-3978.

Respectfully submitted,

Christoph Ruedinger et al.

By: _____

William G. Conger
Registration No. 31,209
Attorney/Agent for Appellant

Date: December 5, 2008

BROOKS KUSHMAN P.C.
1000 Town Center, 22nd Floor
Southfield, MI 48075-1238
Phone: 248-358-4400
Fax: 248-358-3351

Enclosure - Appendices

VIII. CLAIMS APPENDIX

1 - 15. (Cancelled)

16. A process for preparing isocyanatoorganosilanes by thermolysis of carbamatoorganosilanes, wherein the thermolysis takes place with exposure to microwave radiation.

17. The process of claim 16, wherein isocyanatoorganosilanes of the formula (1) are prepared

$$R^2R^3R^4Si\text{-}R^1\text{-}N{=}C{=}O \qquad (1),$$

where

R is a monovalent C_1-C_{10}-alkyl radical,

R^1 is a divalent C_1-C_6-hydrocarbon radical and

R^2, R^3 and R^4 are in each case independently of one another, a methyl, ethyl, n-propyl, isopropyl, methoxy, ethoxy, n-propoxy or isopropoxy radical,

by thermolysis of carbamatoorganosilanes of the formula (2)

$$R^2R^3R^4Si\text{-}R^1\text{-}NH\text{-}CO\text{-}OR \qquad (2).$$

18. The process of claim 16, wherein the thermolysis takes place in the presence of a catalyst.

19. The process of claim 17, wherein no catalyst is present.

20. The process of claim 18, wherein the catalyst is a homogeneous catalyst.

21. The process of claim 20, wherein the catalyst comprises one or more compounds selected from the group consisting of soluble compounds of tin, lead, cadmium, antimony, bismuth, titanium, zirconium, niobium, iron, cobalt, manganese, chromium, molybdenum, tungsten, nickel, copper, zinc, and soluble organic nitrogen bases.

22. The process of claim 20, wherein the catalyst comprises one or more compounds selected from the group consisting of 1,4-diazabicyclo[2.2.2]octane, dibutyltin dilaurate, dibutyltin maleate, dibutyltin diacetate and dimethyltin dichloride.

23. The process of claim 18, wherein the catalyst is a heterogeneous catalyst.

24. The process of claim 23, wherein the catalyst comprises a metal or compound thereof, the metal selected from the group consisting of Sn(I), Sn(II), Pb(II), Zn(II), Cu(I), Cu(II), Co(I), Co(II), Na, K, Li, Rb, Cs, Sr, Ba, Mg, Ca, Cr, Mo, Ti, V, W, Ce, Fe, Ni, Si, Al, Ge, Ga, In, Sc, Y, La and lanthanides, Pd, Pt, Co, Rh, Cu, Ag, Au, Zn, Cr, Mo, W, Cd, Fe, N, O, B, C, and mixtures and alloys containing the abovementioned elements.

25. The process of claim 23, wherein the catalyst comprises at least one oxide, hydroxide, oxyhydroxide, mixed oxide, acetate, formate, oxalate, tartrate, citrate, nitrate, carbonate, or mixtures of the above-mentioned compounds, of one or more elements selected from the group consisting of Sn(I), Sn(II), Pb(II), Zn(II), Cu(I), Cu(II), Co(I), Co(II), Na, K, Li, Rb, Cs, Sr, Ba, Mg, Ca, Cr, Mo, Ti, V, W, Ce, Fe, Ni, Si, Al, Ge, Ga, In, Sc, Y, La and lanthanides, Pd, Pt, Rh, Ag, Au and Cd.

26. The process as claimed in claim 23, wherein the catalyst comprises one or more compounds selected from the group consisting of TiO_2, ZrO_2, HfO_2, Al_2O_3, BaO, CaO, MgO, CeO_2, La_2O_3, Y_2O_3, Sm_2O_3, Yb_2O_3, Cr_2O_3, ZnO, V_2O_4, MnO_2, NiO, In_2O_3, Ga_2O_3, GeO_2, FeO, Fe_2O_3, Fe_3O_4, CuO, Co_3O_4, $Fe(MoO_4)_3$, MgO/CsOH, MgO/NaOH, aluminosilicates, zeolites, cordierite of the composition $2MgO{\cdot}2Al_2O_3{\cdot}5SiO_2$, heteropolyacids, carbon, transition metal nitrides, transition metal borides, transition metal silicides and carbides.

27. The process of claim 23, wherein the catalysts are provided on a support.

28. The process of claim 27, wherein as a catalyst support, an inert refractory material is employed.

29. The process of claim 26, wherein as a catalyst support, oxidic and nonoxidic ceramics, SiO_2, carbon, aluminosilicates, magnesium aluminosilicates or resistant metallic materials are used.

30. The process of claim 26, wherein catalyst supports are in the form of irregular granules, spheres, rings, half-rings, saddles, cylinders, trilobes, or monoliths.

31. The process of claim 16, wherein a gas-phase reactor containing a heterogeneous catalyst is located downstream of the microwave reaction chamber.

IX. EVIDENCE APPENDIX

1. Berger U.S. 3,598,852
2. Sheridan U.S. 6,008,396
3. Mui EP 0 649 850
4. C. Oliver Kappe, MICROWAVES IN ORGANIC AND MEDICINAL CHEMISTRY, Wiley -VCH, pp. 3, 4, 12
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X. RELATED PROCEEDINGS APPENDIX

None

United States Patent Office 3,598,852 Patented Aug. 10, 1971

3,598,852

METHOD OF PREPARING ISOCYANURATE CONTAINING ORGANOSILICON MATERIALS

Abe Berger, Schenectady, N.Y., assignor to General Electric Company

No Drawing. Original application Sept. 20, 1967, Ser. No. 669,298, now Patent No. 3,494,951. Divided and this application Aug. 15, 1969, Ser. No. 870,718
Int. Cl. C07f 7/02, 7/04
U.S. Cl. 260—448.2E 2 Claims

ABSTRACT OF THE DISCLOSURE

A method is provided for making various nitrogen-containing organosilicon compounds, such as silylorganoisocyanates, the corresponding carbamate and isocyanurates. The method involves contacting silylorganohalide and a metal cyanate in the presence of a suitable aprotic solvent. Nitrogen-containing organosilicon compounds are provided having silicon and nitrogen atoms separated by a divalent hydrocarbon radical. In instances where a urethane is desired, an appropriate aliphatic monohydric alcohol can be utilized in combination with the silylorganohalide and metal cyanate. The subject nitrogen-containing organosilicon compounds can be utilized for making silicon-organic copolymers and as treating agents for imparting water repellency to various substrates.

This application is a division of copending application Ser. No. 669,298 filed Sept. 20, 1967, now U.S. Pat. No. 3,494,951.

The present invention relates to various methods of making certain nitrogen-containing organosilicon materials, based on contacting a metal cyanate and a silylorganohalide at elevated temperatures. More particularly, the present invention relates to certain silylorganocarbamates and to the employment of these materials to make silylorganoisocyanates.

Prior to the present invention, methods for making certain silylisocyanates involved the direct reaction between a halosilane and a metal cyanate. For example, Klein Pat. 2,532,559 shows the use of lead cyanate with dimethyldichlorosilane to produce dimethyldiisocyanatosilane. Those skilled in the art know that such silylisocyanates are hydrolytically unstable because the isocyanate radical is directly attached to silicon. Speier Pat. 3,170,-891 shows a method for making silylorganoisocyanates having the silicon atom and the isocyanate radical separated by a divalent hydrocarbon radical. Reaction is effected between a silicon hydride and an olefinically unsaturated isocyanate, such as allylisocyanate. Experience has shown that although the silylorganoisocyanates made by Speier's method, having a silicon-carbon bond, instead of a silicon-nitrogen bond, have improved hydrolytic stability, the method of Speier is undesirable for a variety of reasons. For example, it has been found that silicon hydride addition of a silane to an olefinically unsaturated isocyanate, where the silicon has reactive radicals, such as alkoxy attached to silicon, often results in undesirable side reactions between the alkoxy radicals and isocyanate radicals. In addition, Speier's method is economically unattractive because of the expense of olefinically unsaturated isocyanates, such as allylisocyanate.

The present invention is based on the discovery that silylorganoisocyanates of the formula,

(1) $$(RO)_{3-a}R'_aSiR''NCO$$

can be made by effecting the pyrolysis of the corresponding carbamate as shown by the following equation

$$(RO)_{3-a}R'_aSiR''NHCOR \xrightarrow[\Delta]{} \text{Formula(1)} + ROH$$

where R is an alkyl radical having from 1 to 8 carbon atoms, R' is selected from monovalent hydrocarbon radicals, and halogenated monovalent hydrocarbon radicals, R'' is selected from divalent hydrocarbon radicals and halogenated divalent hydrocarbon radicals, and a is a whole number equal to from 0 to 3, inclusive.

There is provided by the present invention, a method for making silylorganoisocyanates of Formula 1, which comprises (1) heating a silylyorganocarbamate of the formula,

(2) $$(RO)_{3-a}R'_aSiR''NHCOR$$

to a temperature which is sufficient to produce a mixture consisting essentially of (A) said silylorganocarbamate, (B) said silylorganoisocyanate of Formula 1, and (C) an aliphatic monohydric alcohol, (2) continuously distilling said mixture of (1) to provide for the continuous separation of overhead product consisting essentially of (B) and (C) and (3) recovering (B) from said overhead product of (2), where R, R', R'' and a are as previously defined.

The present invention also is directed to silylorganocarbamates of the Formula 2, which can be made by (1) effecting reaction between a silylorganohalide, a metal cyanate and an aliphatic monohydric alcohol in the presence of an aprotic solvent, as shown by the following equation,

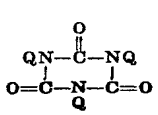
$$(RO)_{3-a}R'_aSiR''X+ROH+M(NCO)_y \rightarrow \text{formula(2)} + MX$$

(2) separating metal salts from the resulting mixture of (1) and (3) stripping the aprotic solvent from the resulting mixture of (2), where R, R', and R'' are as defined above, X is a halogen radical, M is a metal, and y is the valence of the metal.

Radicals included by R of the above formulae are, for example, alkyl radicals, such as methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, and octyl. Radicals included by R' are, for example, aryl radicals and halogenated aryl radicals, such as phenyl, chlorophenyl, xylyl, napthyl, etc.; aralkyl radicals such as benzyl, phenylethyl, etc.; alkyl radicals such as methyl, ethyl, propyl, hexyl, etc.; haloalkyl radicals such as chloropropyl, difluoropropyl, bromobutyl, etc.; alkenyl radicals such as vinyl, allyl, 1-propenyl, etc.; cycloaliphatic and haloaliphatic radicals such as cyclobutyl, cyclopentyl, cyclohexyl, etc. Radicals included by R'' are, for example, alkylene radicals and haloalkylene radicals such as methylene, ethylene, trimethylene, butylene, pentylene, halobutylene, etc.; arylenealkylene such as $-C_6H_4CH_2-$, etc. In the above formulae, where R, R' and R'' can be more than one radical, these radicals can be all the same, or any two or more of the aforementioned radicals.

Another aspect of the invention is directed to a method for making isocyanurates of the formula,

(3)



where Q is $(RO)_{3-a}R'SiR''-$, which comprises (1) effecting reaction between $(RO)_{3-a}R'_aSiR''X$ and $M(NCO)_y$ in the presence of an aprotic solvent (2) removing metal salts from the resulting mixture of (1), and (3) stripping said aprotic solvent from the resulting product of (2)

Included by the silylorganoisocyanates of the Formula 1 are, for example, trimethoxysilylpropylisocyanate, phenyldiethoxysilylpropylisocyanate, methyldimethoxysilylbutylisocyanate, ethoxydimethylsilylbutylisocyanate, etc. Some of the silylorganocarbamates of Formula 2 are, for example, methyl N-trimethoxysilylpropylcarbamate, ethyl N-methyldimethoxysilylpropylcarbamate, ethyl N-triethoxysilylbutylcarbamate, methyl N-phenylmethylmethoxysilylpropylcarbamate, etc.

Alkylhalosilanes which can be utilized in the practice of the invention are, for example, chloropropyltrimethoxysilane, bromopropyltrimethoxysilane, chlorobutyldimethylethoxysilane, chloropropyltriethoxysilane, chloropropylmethyldimethoxysilane, chlorobutylphenylmethyl n-propoxysilane, iodopropyltrimethoxysilane, etc. Metal cyanates which can be employed in the practice of the invention, are for example, lithium cyanate, sodium cyanate, potassium cyanate, rubidium cyanate, barium cyanate, strontium cyanate, silver cyanate, lead cyanate, mercury cyanate, calcium cyanate, etc.

Some of the isocyanurates which are included by Formula 3 are, for example, 1,3,5 - tris(trimethoxysilylpropyl)isocyanurate, 1,3,5 - tris(methyldimethoxysilylpropyl)isocyanurate, 1,3,5 - tris(dimethylethoxysilylbutyl)isocyanurate, 1,3,5-tris(phenylmethylmethoxysilylpropyl)isocyanurate, etc.

The silylorganoisocyanates of Formula 1 can be employed as caulking compounds when exposed to atmospheric moisture. They also can be used to polymerize hydroxylated organic polymers such as polyethers and polyesters. The silylorganocarbamates of Formula 2 can be used as glass sizing materials, metal protectants, etc. Among the uses of the isocyanurates of Formula 3 are as adhesion promoters for room temperature vulcanizing compositions, as shown in my copending application (8DW–450), filed concurrently herewith and assigned to the same assignee as the present invention.

In preparing the silylorganocarbamates of Formula 2, the silylorganohalide, aliphatic monohydride alcohol and metal cyanate are mixed together in a suitable aprotic solvent. Alcohols which can be employed are, for example, methyl alcohol, ethyl alcohol, n-propyl alcohol, n-butyl alcohol and other alcohols having from 1 to 8 carbon atoms. A suitable aprotic solvent is a solvent for the various ingredients required in the practice of the invention, which have no active protons which may interfere with the formation of desired product. Examples of aprotic solvents which can be employed in the practice of the invention are preferably, for example, dimethylformamide, dimethylacetamide, N-methylpyrrolidone, diethylacetamide, and diethylformamide. In addition, solvents such as ethers, nitriles and ester, are operative, such as for example, ethyleneglycoldimethylether, diethyleneglycoldimethylether, triethyleneglycoldimethylether, and tetraethyleneglycoldimethylether, benzonitrile, ethyl benzoate, tributylphosphate, etc. The order of addition of the various reactants is not critical. In order to avoid undesirable losses of reactants, as well as provide for optimum yields of desired product, substantially equal molar amounts of the various reactants, for example, silylorganohalide alcohol, metal cyanate, etc. can be employed even though excesses, such as up to 10 molar excesses of any of the reactants, will not adversely affect the formation of desired product. In instances where a metal cyanate of a polyvalent metal is employed, sufficient metal cyanate should be utilized to provide for at least one mole of cyanate, per mole of silylorganohalide.

After the various ingredients have been mixed together, the resulting mixture can be brought to reflux to initiate the reaction. Experience has shown that a temperature in the range of between 90° C. to 140° C. will generally provide for effective results. Reaction times of from 3 hours to 8 hours will be required depending upon the type and nature of the various reactants employed, and the temperature utilized during the reaction. One indication of

carbamate formation is the rise in the reflux temperature as the urethane starts to form. If desired, a vapor phase chromatograph of the reaction mixture can be taken to confirm the disappearance of starting silylorganohalide and the appearance of the silylorganocarbamate.

The conversion of the silylorganocarbamate to the corresponding isocyanate can be readily achieved. The silylorganocarbamate can be cracked by heating it to reflux under reduced pressure to provide for the initial separation of the aliphatic monohydric alcohol. For example, pressure such as 0.25 mm. to 500 mm. can be employed, while a temperature in the range of 75° C. to 200° C. has been found effective. The alcohol can be caught in a trap, such as a Dry Ice trap. With proper adjustment of the reflux ratio, there can be achieved continuous cracking of the silylorganocarbamate, and continuous separation of the silylorganoisocyanate as an overhead product. The cracking temperature of the silylorganocarbamate and the proper reflux ratio can be best determined by initially bringing the silylorganocarbamate to reflux in a suitable fractionating column under reduced pressure, while providing for the continuous separation of the aliphatic monohydric alcohol.

Experience has shown that if the silylorganocarbamate is heated too rapidly, i.e., without proper reflux control to provide for the separation of overhead product and return of silylorganocarbamate, isocyanurate of Formula 3 can be formed along with isocyanate of Formula 1. To avoid isocyanurate formation, careful control of the reflux of the silylorganocarbamate must be observed.

The preferred method of making the isocyanurate of Formula 3 is by heating a mixture of the silylorganohalide and metal cyanate and an aprotic solvent to a temperature between 100° C.–250° C. and preferably 130–160° C. in the absence of the aliphatic monohydric alcohol. Prior to stripping the isocyanurate of aprotic solvent, removal of metal salts from the mixture has been found expedient.

In order that those skilled in the art may be better able to practice the invention, the following examples are given by way of illustration and not by way of limitation. All parts are by weight.

EXAMPLE 1

A dimethylformamide solution of a mole of chloropropyltrimethoxysilane, 1.2 moles of potassium cyanate and 2 moles of methanol was heated to reflux. The solution consisted of two parts of solvent, per part of the total weight of reactants. The mixture was refluxed for a period of 6 to 8 hours. The temperature of the mixture gradually climbed from 90° C. to 120° C. A vapor phase chromatograph of the mixture showed almost the complete absence of the chloropropyltrimetoxysilane. The mixture was refluxed for an additional two hours. The mixture was then allowed to cool and it was filtered. The solvent was then flashed distilled. The resulting material was then fractionated. There was obtained an 85% yield of a product having a boiling point of 90° C. at 1.4 mm. Hg. Based on method of preparation and its infrared spectrum, the product was methyl N-trimethoxysilylpropylcarbamate.

Methyl N-trimethoxysilylpropylcarbamate is applied to glass fibers by spraying them with a 2% methanol solution. The treated fibers are then heated in contact with a sheet of silicone rubber under pressure. A glass reinforced rubber composite is produced.

EXAMPLE 2

There was heated to 160° C., 119 parts of methyltrimethoxysilylpropylcarbamate. A vacuum of 1 mm. was maintained during the heating. The mixture began to reflux, and a first reaction product was continuously recovered overhead at a temperature of 84° C. In addition, a more volatile second product was continuously caught in a Dry Ice trap. Reflux and product recovery was continued for an additional five hours. There was obtained 75 parts of the first reaction product. Based on its method of preparation, its infrared spectrum showing iso-

cyanate absorption at 4.58 microns, and the total absence of urethane absorption at 5.78 microns, the first reaction product was trimethoxysilylpropylisocyanate.

EXAMPLE 3

A mixture of 40 parts of chloropropyltrimethoxysilane, 50 parts of anhydrous dimethylformamide and 16.2 parts of potassium cyanate was heated to 130° C. at atmospheric pressure. After heating for 4 hours a vapor phase chromatograph showed the complete absence of the original starting material. The reaction mixture was then allowed to cool and it was filtered. It was then stripped of solvent. The resulting product was distilled at 236° C. at 0.2 mm. Hg. There was obtained 35 parts of product which represented a yield of about 86% based on the starting reactants. Based on its method of preparation and its infrared spectrum, the product was 1,3,5-tris(trimethoxysilylpropyl)isocyanurate.

EXAMPLE 4

A mixture of 36.4 parts of chloropropyldimethoxymethylsilane, 16.2 parts of potassium cyanate and 50 parts of dimethylformamide, was heated in accordance with the procedure of Example 3. After a period of about 5 hours at 140° C., a vapor phase chromatograph of the mixture showed the complete absence of the original starting materials. There was obtained a yield of about 82% of product which was distilled at 221° C. at 0.25 mm. Hg. Based on its method of preparation and its infrared spectrum, the product was 1,3,5-tris(dimethoxymethylpropyl)isocyanurate.

EXAMPLE 5

A reaction mixture consisting of 36.4 parts of chloropropylmethyldimethoxysilane, 17 parts of potassium cyanate, 6.4 parts of anhydrous propanol and 75 parts of dry dimethylformamide is allowed to reflux at atmosheric pressure under a dry atmosphere. The reflux temperature rises from 90° C. to 125° C. for a period of about 6 hours. A vapor phase chromatograph shows complete absence of starting material and appearance of a new peak. A product is recovered following the procedure of Example 1. It is propyl N-dimethoxysilylpropylcarbamate, based on its method of preparation and its infrared spectrum.

Propyl N - dimethoxysilylpropylcarbamate is then heated under reduced pressure and fractionated. Propanol is collected in a Dry Ice trap. A second product distills overhead. Based on its method of preparation and its infrared spectrum showing a strong absorption band at 4.58 microns, the product is methyldimethoxysilylpropylisocyanate.

EXAMPLE 6

A carbamate reaction mixture of 29.2 parts of p-phenyldimethoxysilylchloromethylbenzene, 11.1 parts of barium cyanate, 5 parts of methanol and 75 parts of N-methylpyrrolidone is heated to reflux. The p-phenyldimethoxysilylchloromethylbenzene is prepared by initially reacting one mole of p-tolyl magnesium chloride with two moles of phenyltrichlorosilane in tetrahydrofuran at a temperature between 40° C.–60° C. The resulting phenyl, p-tolyl substituted dichlorosilane is thereafter cholrinated

in the presence of ultraviolet light and alkoxylated with methanol in the presence of pyridine.

The course of the above described carbamate reaction is followed with a vapor phase chromatograph. At the completion of the reaction, the mixture is allowed to cool and filtered of salts. The solvent is removed by flash distillation. Based on method of preparation, there is obtained methyl - N - 4 - dimethoxyphenylsilylbenzyl carbamate.

While the foregoing examples have of necessity been limited to only a few of the very many variables within the scope of the present invention, it should be understood that the present invention covers a much broader class of silylorganocarbamates as shown by Formula 2, and methods for making the corresponding isocyanates of Formula 1, and isocyanurates of Formula 3.

What I claim as new and desire to secure by Letters Patent of the United States is:

1. A method for forming isocyanates comprising (a) mixing a silylorganohalide of the formula,

$$(RO)_{3-a}R'_aSiR''X$$

where R is an alkyl radical, R' is selected from monovalent hydrocarbon radicals and halogenated monovalent hydrocarbon radicals, R'' is selected from divalent hydrocarbon radicals and halogenated divalent hydrocarbon radicals, X is a halogen radical and a is a whole number from 0 to 3, inclusive, with a metal cyanate of the formula,

$$M(NCO)_y$$

where M is a metal selected from lithium, sodium, potassium, rudibium, barium, strontium, silver, lead, mercury and calcium, and where y is the valence of the metal, (b) heating the mixture to a temperature sufficient to effect reaction between the silylorganohalide and the metal cyanate in the presence of an aprotic solvent, (c) separating metal salts from the reacted mixture, and (d) stripping said aprotic solvent from the unreacted mixture.

2. A method in accordance with claim 1, which comprises (a) heating a mixture of chloropropyltrimethoxysilane and potassium cyanate to a temperature up to 250° C. at atmospheric pressure in dimethylformamide, (b) separating potassium salts from the mixture of (a) and (c) stripping dimethylformamide from the mixture of (b).

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TOBIAS E. LEVOW, Primary Examiner

W. F. W. BELLAMY, Assistant Examiner

U.S. Cl. X.R.

260—448.2N, 448.8R

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United States Patent [19]

Sheridan et al.

[11] **Patent Number: 6,008,396**

[45] **Date of Patent: Dec. 28, 1999**

[54] **HOT OIL PROCESS FOR PRODUCING ISOCYANATO ORGANOSILANES**

[75] Inventors: **Robert E. Sheridan**, Marietta, Ohio; **Kenneth W. Hartman**, Middlebourne, W. Va.

[73] Assignee: **OSI Specialties, Inc.**, Greenwich, Conn.

[21] Appl. No.: **09/039,052**

[22] Filed: **Mar. 13, 1998**

Related U.S. Application Data

[60] Provisional application No. 60/043,660, Apr. 11, 1997.

[51] **Int. Cl.**[6] **C07F 7/10**

[52] **U.S. Cl.** **556/414**

[58] **Field of Search** 556/414

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Primary Examiner—Paul F. Shaver
Attorney, Agent, or Firm—Edward K. Welch; Timothy X. Witkowski; Andrew S. Reiskind

[57] **ABSTRACT**

Disclosed is a process for making isocyanatoorganosilane by adding a carbamatoorganosilane of the general formula to an inert liquid medium and holding the mixture thus formed at a temperature and pressure effective to convert said carbamatoorganosilane to isocyanatoorganosilane.

10 Claims, No Drawings

HOT OIL PROCESS FOR PRODUCING ISOCYANATO ORGANOSILANES

This application is a continuation of provisional application 60/043,660 filed Apr. 22, 1997.

BACKGROUND OF THE INVENTION

There has been a continuing need for an economical method of preparing isocyanatoorganosilanes, including isocyanatoalkylsilanes, in high yields and purities from relatively non-hazardous raw materials. Heretofore, isocyanatoorganosilanes have been made in relatively low volumes by inefficient or costly processes.

For example, isocyanatoorganosilanes have been prepared by processes involving the addition of hydrosilanes to unsaturated isocyanates, particularly allyl isocyanate, in the presence of a noble metal catalyst. Allyl isocyanate is a highly toxic raw material of limited commercial availability.

Processes also are known wherein isocyanatoalkylsilanes are prepared from carbamatoalkylsilanes at low temperature in the liquid phase, or from aminoalkylsilanes and highly toxic phosgene by various routes. All liquid phase processes disclosed thus far suffer from one or more disadvantages of low yield, slow kinetics, need for highly toxic raw materials, need for extensive work-up or purification, often in the presence of higher levels of close-boiling contaminants, and substantial generation of by-products and waste materials.

High temperature, vapor phase processes are also known; but these generally require specialized equipment capable of high temperature operation, with concurrent extensive capital investment. A method for making 2-isocyanatoethoxysilanes by liquid phase thermal rearrangement of N-silyl-2-oxazolidinones has also been disclosed. The bonding of the isocyanatoalkyl groups to silicon atoms in these molecules is through hydrolyzable silicon-oxygen bonds, and the silane moiety does not contain additional alkoxy groups as are present and often necessary in current commercially useful isocyanatoalkylsilanes.

BRIEF SUMMARY OF THE INVENTION

The present invention provides a method of preparing isocyanatosilanes by the addition of a carbamatoorganosilane to an inert liquid medium at elevated temperatures and reduced pressures effective to decompose the carbamatoorganosilane to the corresponding isocyanatoorganosilane. Isocyanatoorganosilanes that can be prepared include those of the formula $R_x(R'O)_{3-x}SiR''NCO$ (I) wherein x is 0, 1, 2, or 3, each R separately represents a hydrocarbon of 1 to 15 carbon atoms, each R' is separately R, a silyl group R_3Si—, or a siloxy group $R_3Si(OSiR_2)_m$— wherein m is 1 to 4, or when x is 0 or 1 two R' groups together may form a divalent siloxy group —$R_2(OSiR_2)_n$— wherein n is 3 to 5 thus forming a cyclic siloxane, R" represents a divalent hydrocarbon group of 1 to 20 carbon atoms, wherein R, R' and R" may also contain heteroatom functional groups such as ether, thioether, sulfone, ketone, ester, amide, nitrile, or halogen.

DETAILED DESCRIPTION OF THE INVENTION

Adding carbamatosilanes to a hot, inert liquid medium, yields isocyanatoorganosilanes in high yields and purities with no need to use reaction aids, such as highly toxic phosgene or allyl isocyanate, with no generation of highly corrosive hydrogen chloride as a by-product and with minimal formation of other by-products, contaminants, and waste materials. Because the method can be operated continuously with short residence times, a relatively small reactor is capable of large throughputs with a correspondingly small capital investment.

The method of the present invention also can provide isocyanatoorganosilanes in which the isocyanate groups are attached to silicon atoms through branched hydrocarbon groups (R"). Such compounds have isocyanate groups with varying degrees of reactivity, which provide corresponding desirable variations in the performance properties of products incorporating said isocyanatoorganosilanes, including wet strengh, flexibility, and oxidation resistance.

The method of the present invention also can provide isocyanatoorganosilanes wherein the silicon atom bearing the isocyanatoorgano group is further substituted by siloxy groups. These compounds combine the high surface activity of low molecular weight siloxanes with the high reactivity of the isocyanate group, and are useful in providing improved coatings, particularly for metallic substrates such as automobiles.

The liquid reaction medium must be inert, i.e., it is chemically stable in the absence of oxygen at the temperature and pressure at which the reaction is carried out, it exhibits a boiling point higher than that of the isocyanatoorganosilane and it does not boil at the temperature and pressure at which the reaction described herein is carried out. In addition, the liquid medium must either be inert to the reactant carbamatoorganosilane and the product isocyanatoorganosilane, or be rendered inert to the reactant and product by reaction of the liquid medium with the carbamatoorganosilane or the isocyanatoorganosilane. By "rendered inert" is meant that the liquid medium can react with, for instance, the reactant carbamatoorganosilane, such that the liquid medium is converted into another product which functions as a satisfactory inert liquid medium for the reaction described herein. Such reaction consumes only a small portion of the carbamatoorganosilane, given the relatively high ratio of the liquid medium to the reactant.

The liquid medium can be any organic liquid satisfying these conditions, such as hydrocarbons and mixtures of hydrocarbons, unsubstituted or substituted, and optionally containing oxygen or other hetero atoms. Examples include linear and branched alkanes, esters, ethers, cycloaliphatic and aromatic hydrocarbons, fluorocarbons, fluorocarbon ethers, and silicone fluids. Specific examples are HE-200 Vacuum Pump Oil, stripped DARADINE® 68 refined petroleum oil, MULTITHERM® IG-2 refined paraffinic distillate, KRYTOX 107 perfluoropolyether, CHEMTHERM® 700 isomeric dibenzyl toluenes, and SYLTHERM® 800 polysiloxane. Particularly useful are the heat transfer fluids which are commercially available through various sources.

An example of a liquid medium which can be rendered unreactive under the reaction conditions would be a hydroxy terminated polyether. Under the reaction conditions a hydroxyl group would react with either the isocyanate or the alkoxysilicon functionality. In either case the reaction will result in an endcapped polyether which is inert to further reaction.

Many of the liquid media described are available as mixtures of isomers or with a distribution of molecular weights. Some portion of the liquid medium may distill under the reaction conditions. The light ends of these compounds may be allowed to co-distill with the desired isocyanatoorganosilane which is further refined at a later date if needed, or the liquid medium can be pre-stripped of their lower boiling components before use.

The method of the present invention involves the thermal decomposition in the liquid phase, generally at ambient or reduced pressure, of carbamatoorganosilane of the general formula

$$R_x(R'O)_{3-x}SiR''NHCO_2R \quad (II)$$

wherein R, R', R", and x are as defined above. While the R and R' groups may vary within the product isocyanatoorganosilane or starting carbamatoorganosilane molecules, the R and R' groups attached to the oxygen atoms in the isocyanatoalkylsilanes will generally, but not necessarily, be the same.

Preferably R is a lower alkyl of 1 to 4 carbon atoms, but may also be isopropyl or t-butyl to provide for slower hydrolyzation of the silane. Preferably R' is an alkyl group or halogenated alkyl group of 1 to 12 carbon atoms, a cycloalkyl group or halogenated cycloalkyl group of 5 to 8 carbons, an aryl group of 6 to 14 carbons, or an alkaryl or aralkyl group of 7 to 15 carbons. More specifically R' is a lower alkyl of 1 to 4 carbon atoms, or a branched alkyl of 3 to 5 carbon atoms. R" preferably is a linear or branched divalent saturated or unsaturated hydrocarbon group of 1 to 20 carbon atoms attached to silicon by a silicon-carbon bond, including linear and branched alkylene, arylene, alkarylene, and aralkylene groups. Specific examples of R" are $(CH_2)_m$ wherein m=1 to 20, propylene, butylene and phenyl-butylene.

Thus, the method is represented by the following general equation:

$$R_x(R'O)_{3-x}SiR''NHCO_2R \xrightarrow{\text{Inert Solvent/Heat}} R_x(R'O)_{3-x}SiR''NCO + ROH$$

wherein R, R', R", and x are defined as above.

Preferably the reaction is conducted at an elevated temperature between 200° to 400° C., more preferably 250° to 350° C. The pressure of reaction should be at about 10 to about 200 mm Hg, but preferably the pressure is between 30 to 150 mm Hg.

The carbamate silane is added to the solvent wherein the solvent is hot enough to convert the carbamate to the isocyanate. Thus, the amount of carbamate to solvent at any time is small (<5 wt-%) because as soon as the carbamate touches the solvent it will convert to the isocyanate. Thus, as long as there is an excess of solvent, (e.g.,>85% by volume), then this will occur. The carbamate and solvent preferably should not be combined and then heated.

The method of the present invention can be run in a semi-continuous fashion in any flow through apparatus having the capacity for maintaining an inert atmosphere or a reduced pressure, for maintaining a liquid level, and having the capacity to heat the liquid to the desired temperature range, the ability to feed the carbamatoorganosilane into the heated liquid, for removing the ROH byproduct, a column for rectification of the product, if needed, and condensing the desired isocyanatoorganosilane. Said types of apparatus with various capacities are readily available within the chemical industry and can be operated without additional capital expense.

Preferably there is a distillation column attached to the reactor such that the volatile isocyanate silane comes off the reaction system, and unreacted carbamate silane, if any, is returned to the reaction system. Moreover, the alcohol produced in this reaction should be flashed off the product and through the condenser.

Under optimal conditions, the method of the present invention provides isocyanatoorganosilane products requiring no further purification for industrial use. Where an impurity is present, the impurity is either a component of the liquid medium or the starting carbamatoorganosilane, which can typically be removed by simple distillation and recycled if desired.

The starting carbamate silanes may be made as is known in the art. For example, from an amino silane and chloroformate, from a dialkylcarbonate and an amino silane or from a chloroalkyl silane and sodium cyanate in the presence of an alcohol.

The products of the method of the present invention, namely isocyanatoorganosilanes, and particularly $(MeO)_3Si(CH_2)_3NCO$ and $(EtO)_3Si(CH_2)_3NCO$, with numerous uses in manufacturing industries. One use, for example, is in the preparation of silane-grafted polymers as disclosed in U. S. Pat. Nos. 4,113,691 and 4,146,585.

EXAMPLES

Example 1

Production of gamma-isocyanatopropyltrimethoxysilane from methyl carbamatopropyltrimethoxysilane.

To a 4-neck 1 liter round bottom flask fitted with a 10 plate Oldershaw column and a distillation head, a thermometer, and magnetic stir bar were charged 201 grams of HE-200 Vacuum Pump Oil (Leybold Vacuum Products, Inc., Export, Pa.), which is a refined petroleum oil. The oil was heated to a temperature of 315° C. and the system's pressure reduced to 70 mmHg. The condenser coolant temperature was set at 50° C. Methyl carbamatopropyltrimethoxysilane was pumped into the reactor at a rate of 1.26 to 2.61 grams per minute. A short time after the feed was started the head temperature rose to approximately 134° C. and product take off started using a 1:1 reflux ratio. These conditions were maintained until 282 grams of the carbamnate had been fed. A toal of 225 grams of product were collected overhead having an average purity of 98.6% gamma-isocyanatopropyltrimethoxysilane (93.2% reaction yield) as determined by gas chromatographic analysis.

Example 2

Production of gamma-isocyanatopropyltriethoxysilane from ethyl carbamatopropyltriethoxysilane.

This reaction was run as per Example 1, but with the following changes:

The reaction flask was charged with 206 grams of stripped DARADINE® 68 (Dryden Oil Co.) a refined petroleum oil used as a vacuum pump oil) and heated to 340° C. and the system pressure set to 38 mmHg. The starting carbamate, ethyl carbamatopropyltriethoxysilane was fed at a rate of approximately 1.0 grams per minute and product collected overhead using a 4:1 reflux ratio at a head temperature of 144° C. A total of 349 grams of carbamate were fed into the system and 254.4 grams of product was collected having an average purity of 96.6% (83.5% reaction yield) as determined by gas chromatographic analysis.

Example 3

Use of paraffinic distillate as the inert solvent:

The experiment was run as described in Example 1 with the following changes and results:

A total of 92.6 grams of methyl carbamatopropyltrimethoxysilane was fed at a feed rate of 0.86 grams per

minute into 201 grams of MULTITHERM IG-2® (Multitherm Corp., Colwyn, Pa.) refined paraffinic distillate. The pot temperature was maintained at 300–305° C. and the pressure set to 70–75 mmHg. A total of 64.0 grams of product was recovered overhead having an average purity of 96.7% isocyanatopropyltrimethoxysilane (79.9% reaction yield) as determined by gas chromatographic analysis.

Example 4

Use of aromatic hydrocarbon as the inert solvent:

The experiment was run as described in Example 1 with the following changes and results:

A total of 90 grams of methyl carbamatopropyltrimethoxysilane was fed at a feed rate of 1.0 grams per minute into 200 grams of CHEMTHERM 700® (Coastal Chemical Co., Inc., Houston, Tex.) aromatic hydrocarbon containing isomers of dibenzyltoluene. The pot temperature was maintained at 300° C. and the pressure set to 100 mmHg. A total of 90 grams of product was recovered overhead having an average purity of 89.0% isocyanatopropyltrimethoxysilane (90.2% reaction yield) as determined by gas chromatographic analysis.

Example 5

Use of perfluoropolyether as an inert solvent.

The experiment was run as described in Example 1 with the following changes and results:

A total of 152.4 grams of methyl carbamatopropyltrimethoxysilane was fed at a feed rate of 0.5 grams per minute into 202 grams of KRYTOX 107® (E. I. DuPont de Nemours and Co., Wilmington, Del.) perfluoropolyether. The pot temperature was maintained at 342–355° C. and the pressure set to 70 mmHg. A total of 121.8 grams of product was recovered overhead having an average purity of 93.7% isocyanatopropyltrimethoxysilane (86.6% reaction yield) as determined by gas chromatographic analysis.

Example 6

Use of polydimethylsiloxane as the inert solvent:

The experiment was run as described in Example 1 with the following changes and results:

A total of 114 grams of methyl carbamatopropyltrimethoxysilane was fed at a feed rate of 0.5 grams per minute into 200 grams of SYLTHERM 800® (Dow Chemical Co., Midland Mich.), polydimethylsiloxane. The pot temperature was maintained at 295-300° C. and the pressure set to 78 mmHg. A total of 89.4 grams of product was recovered overhead having an average purity of 77.6% isocyanatopropyltrimethoxysilane (70.3% reaction yield) as determined by gas chromatographic analysis.

Example 7

Larger Scale Preparation of gamma-isocyanatopropyltrimethoxysilane from methyl carbamatopropyltrimethoxysilane using MULTITHERM® IG-2 as the inert solvent:

The apparatus consisted of a 200 liter glass kettle, seated in a 4 zone electric heating mantle. The top of the kettle was insulated. A 6 feet×6 inch (182.9 cm×15.2 cm) insulated column was packed with 6 feet (182.9 cm)of Hastelloy packing to make 12–15 theoretical trays. A condenser was at the top of the column with a return to the kettle as well as to one of two 25 liter receiver pots. Tempered water at 60–80° C. was used in the condenser. The kettle contained a glass agitator with 4 blades that were 1.5 inches (3.8 cm) thick & 5 inches (12.7 cm) from tip to tip. An oil driven pump provided the vacuum. Vacuum was measured in the kettle head space.

192 Pounds (71.6 Kg) of MULTITHERM IG-2 were added to the kettle through the heat exchanger to reach a temperature of 120° C. upon entry into the kettle. The oil was heated to 300° C. and the pressure reduced to 70 mmHg. Methyl carbamatopropyltrimethoxysilane was pumped into the oil at an initial rate of 5 pounds/hr (1.9 Kg/hr). During this reaction, the feed rates were varied between 5–10 pounds/hr (1.9–3.7 Kg/hr) with an average feed rate of 5.10 pounds/hr (1.9 Kg/hr). A total of 344 pounds (128.3 Kg) of the carbamate were fed over the 72 hour reaction period yielding gamma-isocyanatopropyltrimethoxysilane with purities on the average >96%.

Example 8

Larger Scale Preparation of gamma-isocyanatopropyltrimethoxysilane from methyl carbamatopropyltrimethoxysilane using recycled Multitherm® IG-2 as the inert solvent:

Multitherm IG-2 previously used to prepare gamma-Isocyanatopropyltrimethoxysilane from methyl carbamatopropyltrimethoxysilane was filtered. 192 Pounds (71.6 Kg) of this recycled oil were added to the apparatus mentioned in example 7. During this reaction, the feed rates were varied between 2.5–5.5 pounds/hr (0.9–2.0 Kg/hr) with an average feed rate of 3.33 pounds/hr (1.2 Kg/hr). A total of 193 pounds (72.0 Kg)of the carbamate were fed over the 71 hour reaction period yielding gamma-isocyanatopropyltrimethoxysilane with purities >96% and on the average >97.5%.

Example 9

Larger Scale Preparation of gamma-isocyanatopropyltriethoxysilane from ethyl carbamatopropyltriethoxysilane using Multitherm® IG-2 as the inert solvent:

This example was similar to example 7 with the exception that ethyl carbamatopropyltriethoxysilane was used as the feed. During this reaction, the feed rates were varied between 1.3–3.6 pounds/hr (0.5–1.3 Kg/hr) with an average feed rate of 3.6 pounds/hr (1.3 kg/hr). A total of 197 pounds (73.5 Kg) of the carbamate were fed over the 55 hour reaction period with purities of gamma-isocyanatopropyltriethoxysilane initially >98% but falling to 90% after 37 hours due to the build up of an impurity.

Comparison with Liquid Phase Cracking in the absence of hot, inert liquid medium:

In a 1 liter 3-neck, round bottomed flask equipped with a 10 plate Oldershaw distillation column, distillation head, and receiver, thermometer, and magnetic stir bar was placed 349.6 grams of methyl carbamatopropyltrimethoxysilane. The pot contents were heated to between 190–204° C. at 52–54 mmHg pressure for a total of 7 hours. During this time a total of 205.3 grams of product was collected overhead in several distillate cuts, having an average purity of 93.1% isocyanatopropyltrimethoxysilane giving the reaction a net yield of 67.3%. The reactor contained 96.9 grams of heavies and the net material balance 96.4%.

Similar liquid phase results were obtained with ethyl carbamatopropyltriethoxysilane as reported in Example A of U.S. Pat. No. 5,393,910, granted to the assignee of the present invention.

What is claimed is:

1. A method comprising adding a carbamatoorganosilane to an inert liquid medium which is at a temperature and pressure effective to convert said carbamatoorganosilane to an isocyanatoorganosilane.

2. A method according to claim 1 additionally comprising isolating the isocyanatoorganosilane formed.

3. A method according to claim 1 wherein the isocyanatoorganosilane is of the formula

$$R_x(R'O)_{3-x}SiR''NCO$$

wherein x is an integer having a value of 0, 1, 2, or 3,

each R separately represents an alkyl group or halogenated alkyl group of 1 to 12 carbon atoms, a cycloalkyl group or halogenated cycloalkyl group of 5 to 8 carbons, an aryl group of 6 to 14 carbons, or an alkaryl or aralkyl group of 7 to 15 carbons,

each R' is separately R or a silyl group R_3Si—, or a siloxy group $R_3Si(OSiR_2)_m$— wherein m is an integer having a value of 1 to 4, or when x is 0 or 1 two R' groups taken together may form a divalent siloxy group —$R_2(OSiR_2)_n$— wherein n is an integer having a value of 3, 4, or 5 thus forming a cyclic siloxane with the silicon atom bearing the isocyanatoorgano group,

R" represents a linear or branched divalent saturated or unsaturated hydrocarbon group of 1 to 20 carbons attached to silicon by a silicon-carbon bond; and

wherein R, R', and R" optionally may contain heteroatom functional groups such as ether, thioether, sulfone, ketone, ester, amide, nitrile, or halogen.

4. A method according to claim 1 wherein the carbamatoorganosilane is of the formula

$$R_x(R'O)_{3-x}SiR''NCO_2R$$

wherein x is an integer having a value of 0, 1, or 2,

each R separately represents an alkyl group or halogenated alkyl group of 1 to 12 carbon atoms, a cycloalkyl group or halogenated cycloalkyl group of 5 to 8 carbons, an aryl group of 6 to 14 carbons, or an alkaryl or aralkyl group of 7 to 15 carbons,

each R' is separately R or a silyl group R_3Si—, or a siloxy group $R_3Si(OSiR_2)_m$— wherein m is an integer having a value of 1 to 4, or when x is 0 or 1 two R' groups taken together may form a divalent siloxy group —$R_2(OSiR_2)_n$— wherein n is an integer having a value of 3, 4, or 5 thus forming a cyclic siloxane with the silicon atom bearing the isocyanatoorgano group,

R" represents a linear or branched divalent saturated or unsaturated hydrocarbon group of 1 to 20 carbons attached to silicon by a silicon-carbon bond,

wherein R, R', and R" may also contain heteroatom functional groups such as ether, thioether, sulfone, ketone, ester, amide, nitrile, or halogen.

5. A process according to claim 1 wherein the liquid medium is a hydrocarbon.

6. A process according to claim 1 wherein the liquid medium is selected from the group coonsisting of vacuum pump oil, stripped refined petroleum oil, refined paraffinic distillate, pefluoropolyether, isomeric dibenzyl toluenes, and polysiloxane.

7. A process according to claim 1 wherein the liquid medium is at a temperature between about 200° and about 400° C.

8. A process according to claim 1 wherein the pressure is between about 10 to about 200 mm Hg.

9. A process according to claim 1 wherein the isocyanatoorganosilane is selected from the group of isocyanatopropyltrimethoxysilane and isocyanatopropyltriethoxysilane.

10. A process according to claim 4 wherein x has a value of 0, 1, or 2, R and R' are selected from the group of methyl and ethyl groups, and R" is a linear propylene group.

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(54) Process for making isocyanatoorganosilanes

Verfahren zur Herstellung von Isocyanatoorganosilanen

Procédé de préparation d'isocyanatoorganosilanes

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(73) Proprietor: **OSi Specialties, Inc.**
Danbury, Connecticut 06810-5121 (US)

(72) Inventors:
- **Mui, Jeffrey, Yick Pui**
  Bellingham, Massachusetts 02019 (US)
- **Bowman, Mark Paul**
  Marietta, Ohio 45750 (US)

(74) Representative:
Wibbelmann, Jobst, Dr., Dipl.-Chem.
Wuesthoff & Wuesthoff,
Patent- und Rechtsanwälte,
Schweigerstrasse 2
81541 München (DE)

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Evidence Appendix 3

Description

The present invention relates to a method of preparing isocyanatoorganosilanes and to certain isocyanatoorganosilanes so prepared.

Background of the Invention

There has been a continuing need for a method of preparing isocyanatoorganosilanes, including isocyanatoalkylsilanes, in high yields and purities from economical and relatively non-hazardous raw materials without generating significant quantities of hazardous by-products and waste materials. Heretofore, isocyanato-organosilanes have been made in relatively low volumes by inefficient or costly processes.

For example, isocyanatoorganosilanes have been prepared by processes involving addition of hydrosilanes to unsaturated isocyanates, particularly allyl isocyanate, in the presence of a noble metal catalyst. Allyl isocyanate is a highly toxic raw material of limited commercial availability.

Processes are also known in the art wherein isocyanatoalkylsilanes are prepared from carbamato-alkylsilanes at a low temperature in the liquid phase, or from aminoalkylsilanes and highly toxic phosgene by various routes. All liquid phase processes disclosed thus far suffer from one or more disadvantages of low yield, slow kinetics, need for highly toxic raw materials, need for extensive work-up or purification often in the presence of higher levels of close-boiling contaminants, and substantial generation of by-products and waste materials.

A method for making 2-isocyanatoethoxysilanes by liquid phase thermal rearrangement of N-silyl-2-oxazolidinones has also been disclosed. The bonding of the isocyanatoalkyl group to silicon atoms in these molecules is through a hydrolyzable silicon-oxygen bond, and the silane moiety does not contain additional alkoxy groups as are present and often necessary in current commercially useful isocyanatoalkylsilanes.

The present invention surprisingly provides a method wherein isocyanatoorganosilanes are provided in high yields and purities with no need to use highly toxic phosgene or highly toxic allyl isocyanate, with no generation of highly corrosive hydrogen chloride as a by-product, with no need to use inert solvents as diluents, and with minimal formation of by-products, contaminants, and waste materials. Because the method of the present invention can be operated continuously with very short residence times, a relatively small reactor is capable of large throughputs with a correspondingly small capital investment.

The method of the present invention can also provide isocyanatoorganosilanes which have not been prepared by methods known to those skilled in the art, including isocyanatoorganosilanes in which the isocyanate groups are attached to silicon atoms through branched hydrocarbon groups. Such branched hydrocarbon groups respond to a need for isocyanatoorganosilanes having isocyanate groups with varying degrees of reactivity, which provide corresponding desirable variations in the performance properties of products incorporating said isocyanatoorganosilanes, including wet strength, flexibility, and oxidation resistance.

The method of the present invention can also provide isocyanatoorganosilanes wherein the silicon atom bearing the isocyanatoorgano group is further substituted by siloxy groups. These compounds combine the high surface activity of low molecular weight siloxanes with the high reactivity of the isocyanate group, and are useful in providing improved coatings, particularly for metallic substrates such as in automotive applications.

Summary of the Invention

The present invention provides a method of preparing isocyanatoorganosilanes. The method simply involves vaporizing a carbamatoorganosilane and heating said vaporized carbamatoorganosilane in a reaction zone at an elevated temperature for a time sufficient to form said isocyanatoorganosilane. Specific isocyanatoorganosilanes that can be prepared include those having the general formula $R_x(R''O)_{3-x}SiR'NCO$ wherein x is an integer having a value of 0, 1, 2, or 3, each R separately represents an alkyl group or halogenated alkyl group of 1 to 12 carbon atoms, a cycloalkyl group or halogenated cycloalkyl group of 5 to 8 carbon atoms, an aryl group of 6 to 14 carbon atoms, or an alkaryl or aralkyl group of 7 to 15 carbon atoms, each R'' separately represents R or a silyl group R_3Si-, or a siloxy group $R_3Si(OSiR_2)_m$- wherein m is an integer having a value of 1 to 4, or when x is 0 or 1 two R'' groups together may form a divalent siloxy group $-R_2(OSiR_2)_n$- wherein n is an integer having a value of 3, 4, or 5 thus forming a cyclic siloxane with the silicon atom bearing the isocyanatoorgano group, and R is as defined above, R' represents a divalent hydrocarbon group of 1 to 20 carbon atoms, preferably a linear or branched divalent saturated or unsaturated hydrocarbon group of 1 to 20 carbon atoms attached to silicon by a silicon-carbon bond, including linear and branched alkylene, arylene, alkarylene, and aralkylene groups, and wherein R and R' may also contain heteroatom functional groups such as ether, thioether, sulfone, ketone, ester, amide, nitrile, or halogen.

The method involves the elevated temperature thermally induced decomposition in the gas phase generally at ambient or reduced pressure of a carbamatoorganosilane of the general formula $R_x(R''O)_{3-x}SiR'NHCO_2R$ wherein R,

R'', R', and x are as defined above. While the R and R'' groups may vary within the product isocyanatoorganosilane or starting carbamatoorganosilane molecules, the R and R'' groups attached to the oxygen atoms in the isocyanatoalkylsilanes will generally, but not necessarily, be the same.

Thus, the method of the present invention is represented by the following general equation:

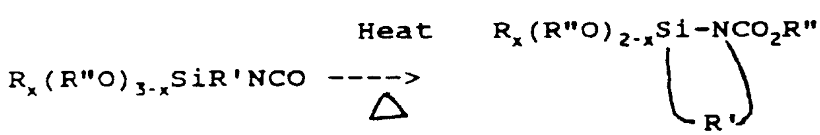
$$R_x(R''O)_{3-x}SiR'NHCO_2R \xrightarrow[\Delta]{\text{Heat}} R_x(R''O)_{3-x}SiR'NCO + ROH$$

wherein R, R'', R' and x are as defined above. Preferably the reaction is conducted at an elevated temperature of 300° to 600° C. The method of the present invention can be performed in continuous fashion in any flow-through apparatus having the capacity for maintaining an inert diluent atmosphere or a reduced pressure, for vaporizing the carbamatoorganosilane raw materials, for providing a heated reaction zone at an elevated temperature, preferably in the range of about 300°-600° C, for removing the ROH by-product, for maintaining physical integrity against the relatively high reaction temperatures, and for minimizing thermal conversion of the isocyanato-organosilanes so formed to silicon-containing ceramic compositions which can accumulate in the apparatus.

While organic hydrocarbon isocyanates have been prepared at high temperatures in flow-through equipment, the use of such a method to convert carbamatoorganosilanes cleanly and at high yield to isocyanatoorganosilanes was unexpected in view of the high temperature thermal conversions of a variety of organosilicon compounds to silicon-containing ceramic compositions, namely silicon carbide, silicon nitride, silicon oxycarbide, and mixtures thereof that one would have expected to occur.

While not wishing to be bound by theory, it may be that the gas phase preparation of isocyanatoorganosilanes can occur at a higher yield than in the prior liquid phase preparation because the gas phase process, in essence, may permit the reaction to proceed more on a unimolecular scale. Vaporization of carbamatoorganosilanes in principle separates each silane molecule from closely bound equivalent molecules as encountered in the liquid phase. Thus, by-product or heavies formation by bimolecular or trimolecular reactions which occur in the liquid phase may be reduced or avoided in the gas phase. Furthermore, applicant has found that the avoidance of any build-up of non-volatile residue in the reactor can be aided by adjusting the rate that the vaporized carbamatoorganosilane is introduced into the reaction zone. The most appropriate rate for a particular reactor depends on a variety of factors, but can readily be determined by one skilled in the art using routine optimization.

One side reaction encountered in the liquid phase but not in the gas phase is the formation of close-boiling cyclic silyl carbamates from isocyanatoorganosilanes, with which they are isomeric. Simply heating isocyanatoorganosilanes, where R'' is a methyl or ethyl group, in the liquid phase to about 140° C causes



significant rearrangement of isocyanatoorganosilane to cyclic silyl carbamate where x is 0, 1, or 2. Correspondingly, isocyanatoorganosilanes prepared in the liquid phase contain significantly higher contents of cyclic silyl carbamates as close-boiling contaminants, compared to the same materials prepared by the present invention.

Under optimal conditions, the method of the present invention provides isocyanatoorganosilane products requiring no further purification for industrial use. Where an impurity is present, the impurity is essentially the starting carbamatoorganosilane, which can be removed by simple distillation and recycled to provide additional product.

The products of the method of the present invention, namely isocyanatoorganosilanes, and particularly $(MeO)_3Si(CH_2)_3NCO$ and $(EtO)_3Si(CH_2)_3NCO$, are articles of commerce, with numerous uses in manufacturing industries. One use, for example, is in the preparation of silane-grafted polymers as disclosed in U.S. 4,113,691 and U. S. 4,146,585.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides a method of preparing an isocyanatoorganosilane by elevated temperature thermally induced decomposition of a carbamatoorganosilane preferably at a temperature in the range of about 300 to 600°C in the gas phase generally under ambient or reduced pressure. Preferably the method is used to prepare an isocyanatoorganosilane having the general formula $R_x(R''O)_{3-x}SiR'NCO$ from a carbamatoorganosilane having the

general formula $R_x(R''O)_{3-x}SiR'NHCO_2R$ according to the equation:

$$R_x(R''O)_{3-x}SiR'NHCO_2R \xrightarrow[\Delta]{\text{Heat}} R_x(R''O)_{3-x}SiR'NCO + ROH$$

wherein x is an integer having a value of 0, 1, 2, or 3, each R separately represents an alkyl group or halogenated alkyl group of 1 to 12 carbon atoms, a cycloalkyl group or halogenated cycloalkyl group of 5 to 8 carbon atoms, an aryl group of 6 to 14 carbon atoms, or an alkaryl or aralkyl group of 7 to 15 carbon atoms, each R'' separately represents R or a silyl group R_3Si-, or a siloxy group $R_3Si(OSiR_2)_m$- wherein m is an integer having a value of 1 to 4, or when x is 0 or 1 two R'' groups together may form a divalent siloxy group -$SiR_2(OSiR_2)_n$-wherein n is an integer having a value of 3, 4, or 5, thus forming a cyclic siloxane with the silicon atom bearing the isocyanatoorgano group, and R is as defined above, R' represents a linear or branched divalent saturated or unsaturated hydrocarbon group of 1 to 20 carbon atoms attached to silicon by a silicon-carbon bond, including alkylene, arylene, alkarylene, and aralkylene groups, and wherein R and R' may also contain heteroatom functional groups such as ether, thioether, sulfone, ketone, ester, amide, nitrile, or halogen. It should be recognized that the R, R', R'', and heteroatom functional groups in the starting materials and products are those which can be subjected to the conditions of the method without adverse chemical change. While the R and R'' groups may vary within the isocyanato-organosilane and carbamatoorganosilane molecules, the R and R'' groups attached to oxygen atoms in said isocyanatoorganosilanes will generally, but not necessarily, be the same.

The method of the present invention generally is performed in continuous fashion in any flow-through apparatus having the capability for maintaining an inert atmosphere, for vaporizing the carbamatoorganosilane raw material, for maintaining a heated reaction zone at an elevated temperature preferably in the range of about 300° to 600° C, for removing the ROH by-product, for maintaining physical integrity against the relatively high reaction temperature, and for minimizing thermal conversion of the isocyanatoorganosilane products so formed to silicon-containing ceramic compositions. The apparatus may be constructed from metal, alloy, glass, or ceramic material, and may be connected to ancillary equipment as needed for feeding the carbamatoorganosilane to the vaporizer/heated reaction zone, and for collecting and optionally purifying the isocyanatoorganosilane products. Reaction conditions are not narrowly critical, since yields can be optimized by adjusting residence times and temperatures in a given apparatus. The method of the present invention can also be operated at atmospheric, subatmospheric, or superatmospheric pressures. However, atmospheric or subatmospheric pressures in the range of $1{,}3 \cdot 10^3$ - $101{,}3 \cdot 10^3$ Pa (10 mm - 760 mm) are normally preferred. Various catalysts are known in the art for catalyzing the decomposition of carbamates to isocyanates and alcohols. However, the use of a catalyst in the method of the present invention is optional.

Thermal input to the carbamatoorganosilane vaporizer and heated reaction zone can be provided by superheated steam, flame furnace, or by electrical heaters, and controlled and measured by standard devices for that purpose. Configuration of such total equipment regarding direction of flow, multiplicity and size of contained flows, and shape or pattern of flow are also not narrowly critical. One assembly of equipment, generally referred to as a hot tube reactor, is well known in the art and is in use in the commercial production of various chemicals which require high temperature process steps in the gas phase.

A preferred apparatus for conducting the process of the present invention on a laboratory scale comprises a stainless steel tube packed with stainless steel saddles. Thermal input is provided electrically. The system can be operated at $40{,}0 \cdot 10^3$ - $101{,}3 \cdot 10^3$ Pa (300 to 760 mm) pressure, with vaporizer temperatures in the 340° to 380° range, and heated reaction zone temperatures in the 400° to 520° range.

It is understood that various mechanical devices known in the art, such as spray nozzles or atomizers, may be used to assist in vaporizing the carbamatoorganosilane raw materials, and that the vaporizer temperature need not be different from that of the temperature prevailing in the reaction zone.

Preferred carbamatoorganosilanes and the resulting isocyanatoorganosilane products are those wherein the R groups have 1 to 4 carbon atoms, and most preferably 1 to 2 carbon atoms. Alkyl groups are preferred, i.e., methyl or ethyl groups. Preferred R'' groups are R groups, trimethylsilyl groups, or divalent siloxy groups, -$SiMe_2(OSiM_2)_n$-, where n is 3 or 4, formed from two R'' groups when x is 1. Preferred R' groups are linear or branched divalent hydrocarbon groups containing 1 to 11 carbon atoms of the formula -C_nH_{2n}-, preferably where n is an integer of 3 to 6, and most preferably the divalent hydrocarbon group -$(CH_2)_3$-. It is understood that the divalent hydrocarbon group -C_nH_{2n}- can be branched, and that the isocyanate group of the product may be attached to a primary, secondary, or tertiary carbon atom. Thus, isocyanatoorganosilanes, $R_x(R''O)_{3-x}SiR'NCO$, wherein R' is selected from the group of -$CH_2CH_2CMe_2$-, -$CH_2CH_2CHMeCH_2$-, -$CH_2CH_2CMe_2CH_2$-, and -$CH_2CHMeCH_2$- where Me is a methyl group, are also preferred em-

bodiments of the present invention. Preferred values of x include 0, 1, and 2, with the values of 0 and 1 being most preferred.

Carbamatoorgaosilanes useful in the method of the present invention for making isocyanatoorganosilanes may be selected from the group of: $(MeO)_3Si(CH_2)_3NHCO_2Me$, $Me(MeO)_2Si(CH_2)_3NHCO_2Me$, $Me_2(MeO)Si(CH_2)_3NHCO_2Me$, $(EtO)_3Si(CH_2)_3NHCO_2Et$, $Me(EtO)_2Si(CH_2)_3NHCO_2Et$, $Me_2(EtO)Si(CH_2)_3NHCO_2Et$, $(PrO)_3Si(CH_2)_3NHCO_2Pr$, $(MeO)_3SiCH_2CHMeCH_2NHCO_2Me$, $Me(MeO)_2SiCH_2CHMeCH_2NHCO_2Me$, $(EtO)_3SiCH_2CHMeCH_2NHCO_2Et$, $Me_2(MeO)SiCH_2CHMeCH_2NHCO_2Me$, $Me(EtO)_2SiCH_2CHMeCH_2NHCO_2Et$, $Me_2(EtO)SiCH_2CHMeCH_2NHCO_2Et$, $(MeO)_3Si(CH_2)_4NHCO_2Me$, $Me(MeO)_2Si(CH_2)_4NHCO_2Me$, $Me_2(MeO)Si(CH_2)_4NHCO_2Me$, $Me(EtO)_2Si(CH_2)_4NHCO_2Et$, $(F_3CCH_2O)_3Si(CH_2)_3NHCO_2Me$, $Me(F_3CCH_2O)_2Si(CH_2)_3NHCO_2Me$, $Me(EtO)_2Si(CH_2)_2CHMeCH_2NHCO_2Et$, $(MeO)_3Si(CH_2)_2CHMeCH_2NHCO_2Me$, $Me(MeO)_2SiCH_2NHCO_2Me$ and the like wherein Me is a methyl group, Et is an ethyl group, and Pr is a propyl group.

The carbamatoorganosilane raw materials may be prepared by any of the variety of methods known in the art, including by reaction of aminoorganosilanes with chloroformate esters, by reaction of hydrosilanes with unsaturated carbamate esters, by reaction of chloroorganosilanes with cyanate salts in the presence of an alcohol, or by reaction of aminoorganosilanes with dialkyl carbonates in the presence or absence of a catalyst. The latter method is the preferred method, and is disclosed in U.S. 5,218,133, assigned to the same assignee as the present invention. It is understood that virtually any aminoorganosilane can be converted to the corresponding carbamatoorganosilane, and said corresponding carbamatoorganosilane can be converted to the corresponding isocyanatoorganosilane by the method of the present invention, with the provisos that the corresponding carbamatoorganosilane be vaporizable and the corresponding isocyanatoorganosilane be stable under the gas phase reaction conditions.

In addition to those aminoorganosilanes used to prepare the specific carbamatoorganosilane structures shown above, aminoorganosilanes leading to carbamatoorganosilanes useful in the method of the present invention also may be selected from the group of: $(MeO)_3Si(CH_2)_2CMe_2NH_2$, $Me(MeO)_2Si(CH_2)_2CMe_2NH_2$, $(MeO)_3Si(CH_2)_2CMe_2CH_2NH_2$, $(EtO)_3Si(CH_2)_2CMe_2CH_2NH_2$, $Me(Meo)_2Si(CH_2)_2CMe_2CH_2NH_2$, $Me_2(EtO)Si(CH_2)_2CMe_2CH_2NH_2$, $(MeO)_3SiCH{=}CHCMe_2NH_2$, $Me(MeO)_2SiCH{=}CHCMe_2NH_2$, $(MeO)_3Si(CH_2)_2C_6H_4CH_2NH_2$, $Me(EtO)_2Si(CH_2)_2C_6H_4CH_2NH_2$, $(EtO)_3Si(CH_2)_3OC_6H_4NH_2$, $Me(MeO)_2Si(CH_2)_3OC_6H_4NH_2$, $(MeO)_3Si(CH_2)_3NHC_6H_4NH_2$, $Me(EtO)_2Si(CH_2)_3NHC_6H_4NH_2$, $Me(Me_3SiO)_2Si(CH_2)_3NH_2$, $(Me_3SiO)_3Si(CH_2)_3NH_2$,

$(MeO)_3Si(CH_2)_{11}NH_2$, $(MeO)_3SiC_6H_4NH_2$, and the like wherein Me and Et are as defined above and C_6H_4 is a phenylene group.

Isocyanatoorganosilanes having the formula $R_x(R''O)_{3-x}SiR'NCO$, wherein R' is a divalent branched hydro-carbon radical of 3 to 11 carbon atoms, preferably one selected from the group of $-CH_2CH_2CMe_2-$, $-CH_2CH_2CHMeCH_2-$, $-CH_2CH_2CMe_2CH_2-$, and $-CH_2CHMeCH_2-$, and R, R'', and x are as defined as above, have not been prepared prior to the present invention. The facile preparation of these molecules by the process of the present invention was unexpected in view of the tendency of branching in the group R' to promote cyclization reactions. For example, the facile cyclization of $(MeO)_3SiCH_2CH_2CMe_2CH_2NH_2$ is disclosed in copending application Serial No. 07/993,304, assigned to the same assignee of the present invention.

The isocyanatoorganosilanes, $R_x(R''O)_{3-x}Si(CH_2)_3NCO$, wherein R'' represents a silyl group R_3Si- or wherein two R'' groups together form a divalent siloxy group $-SiR_2(OSiR_2)_n-$, and wherein R, n, and x are as defined above, possibly can be prepared by prior art methods, but, with the exception of $(Me_3SiO)_3Si(CH_2)_3NCO$, have not been so prepared.

Whereas the exact scope of the present invention is set forth in the appended claims, the following specific examples illustrate certain aspects of the present invention and, more particularly, point out methods of evaluating same. However, the examples are set forth for illustrative purposes only and are not to be construed as limitations on the present invention. The abbreviations g, mol, min, sec, cm, mm, and ca respectively represent gram, molecular equivalent, minute, second, centimeter, millimeter, and about; temperature is reported in degrees Centigrade. Yield and by-product percentages are reported as weight-percent values, corrected by appropriate response factors, as determined by gas chromatography. All reactions were run under an inert atmosphere of nitrogen, or under a reduced pressure.

EXAMPLE 1 - PREPARATION OF 3-ISOCYANATOPROPYLTRIMETHOXYSILANE

Methyl N-(3-trimethoxysilylpropyl)carbamate (1135 g, 4.79 mols) was fed to a vertically mounted stainless steel hot tube reactor, packed with stainless steel saddles and having a volume of 65 cm^3, at a rate of 1.2 g/min. The top of the reactor served as a vaporizer and was maintained at 380° C while the remainder of the reactor was maintained at 520° C. The reactor pressure was maintained at $53{,}3 \cdot 10^3$ Pa (400 mm Hg). Product was collected in an air-cooled flask connected to the lower end of the reactor at ambient temperature. Subambient cooling was achieved by the

removal of methanol from the crude product by the periodic application of vacuum (ca 5 mm Hg). Removing methanol by the intermittent application of a higher vacuum to the air-cooled flask in which product was collected also inhibited any recombination between the isocyanatoorganosilane and the by-product alcohol that might otherwise have occurred. A total of 988 g (4.82 mols, 93% yield) of 3-isocyanatopropyltrimethoxysilane was collected at a purity of 92%, based on gas chromatographic analysis.

EXAMPLE 2 - PREPARATION OF 3-ISOCYANATOPROPYLTRIETHOXYSILANE

Ethyl N-(3-triethoxysilylpropyl)carbamate (52 g, 0.18 mol) was fed to an unpacked stainless steel upflow hot tube reactor having a volume of 66 cm^3 (1.05 cm X 76 cm) at a rate of 2.6 g/min. The vaporizer was maintained at 340° C and the remainder of the hot tube at 460° C. The reactor pressure was maintained at ambient atmospheric pressure. Crude product (49.7 g) was collected, containing 39.1 g (0.16 mol, 89% yield) of 3-isocyanatopropyltriethoxysilane, based on gas chromatographic analysis.

EXAMPLE 3 - PREPARATION OF 3-ISOCYANATOPROPYLMETHYL-DIMETHOXYSILANE

The procedure of Example 1 was followed using the same reactor, temperatures, and pressure. Methyl N-(3-methyldimethoxysilylpropyl)carbamate (15.4 g, 0.07 mol) was fed to the top of the reactor at a rate of 1.0 g/min. 3-Isocyanatopropylmethyldimethoxysilane (11.6 g, 0,06 mol, 76% yield) was collected at a purity of 86% as determined by gas chromatographic analysis.

EXAMPLE 4 - STABILITY TEST OF 3-ISOCYANATOPROPYLTRIETHOXYSILANE

A sample of purified 3-isocyanatopropyltriethoxysilane was passed through the hot tube reactor of Example 2, except that the reactor temperature was 465° C and the pressure was $40{,}0 \cdot 10^3$ Pa (300 mm) Hg. The residence time in the reactor was 3.0 sec. Only 2.5 % of close-boiling by-products were formed, with no formation of uneluted heavies by gas chromatographic analysis. This example shows that products of the process of the present invention are stable in the hot tube reactor under reaction conditions, and that uneluted heavies are not formed from said products under reaction conditions.

EXAMPLE 5 - PREPARATION OF 3,3-DIMETHYL-4-ISOCYANATO-BUTYLMETHYLDIMETHOXYSILANE

Methyl N-(2,2-dimethyl-4-methyldimethoxysilylbutyl)carbamate, $Me(MeO)_2SiCH_2CH_2CMe_2CH_2NHCO_2Me$ (18.4 g) , was passed through the apparatus of Example 1 at a rate of 1.4 g/min at $53{,}3 \cdot 10^3$ Pa (400 mm) Hg with the vaporizer at 350°C and the hot tube at 590°C. The product was stripped under vacuum to yield 15.6 g of $Me(MeO)_2SiCH_2CH_2CMe_2CH_2NCO$ (85 % purity by gas chromatographic analysis, 82% yield).

COMPARATIVE EXAMPLE A - LIQUID PHASE PREPARATION OF 3 -ISOCYANATOPROPYLTRIETHOXYSILANE

Ethyl N-(3-triethoxysilylpropyl)carbamate (348.7 g, 1.19 mols) was heated at 200° C for 5 hours at $6{,}7 \cdot 10^3$ Pa (50 mm Hg) pressure. The glass flask reactor was fitted with a 10 tray Oldershaw distillation column to remove the isocyanatoalkylsilane product to a receiver as it was formed. Product cuts were collected at 149-156° C/$6{,}7 \cdot 10^3$ Pa (50 mm Hg) totalling 218.5 g, containing 210 g of 3-isocyanatopropyltriethoxysilane (71% yield), plus a mid-cut at 154-168° C/$6{,}7 \cdot 10^3$ Pa (50 mm Hg) (38.9 g) which contained only 51.6% of 3-isocyanatopropyltriethoxysilane, with 11.1% of cyclic silyl carbamate, 18.5% of starting carbamate, and 17.5% of uneluted heavies by gas chromatographic analysis. If the 3-isocyanatopropyltriethoxysilane in this crude mid-cut is added to that in the purer cuts, the total yield is 78.3%, which compares well with the 72.9% yield calculated from Example 2, U.S. 3,607,901, also a liquid phase example. This example, and that of U.S. 3,607,901, of liquid phase preparation of isocyanatoorganosilanes, show that yields are lower and contents of close-boiling cyclic silyl carbamate contaminants are higher than those of the present invention, which is a gas phase process.

COMPARATIVE EXAMPLE B - LIQUID PHASE STABILITY OF 3-ISOCYANATOPROPYLTRIETHOXYSILANE

A sample of 3-isocyanatopropyltriethoxysilane, as prepared in Comparative Example A, was heated under an inert atmosphere at 140° C. After 6 hours, the purity had dropped to 85.6 %, with 12.1% of cyclic silyl carbamate being present. After 2 days at 140° C, the sample contained 57.8% of heavies, as determined by gas chromatographic analysis. This example, in conjunction with Example 4 of the present invention, shows that isocyanatoorganosilanes are much less stable under liquid phase conditions than they are under gas phase conditions even though temperatures

are much higher under gas phase conditions.

The principles, preferred embodiments, and modes of operation of the present invention have been described in the foregoing specification. The invention which is intended to be protected herein, however, is not to be construed as limited to the particular forms disclosed, since they are regarded as illustrative rather than restrictive.

Claims

1. A method for preparing an isocyanatoorganosilane comprising vaporizing a carbamatoorganosilane and heating said vaporized carbamatoorganosilane in a reaction zone at an elevated temperature for a time sufficient to form said isocyanatoorganosilane.

2. The method of Claim 1 wherein the isocyanatoorganosilane has the formula $R_x(R''O)_{3-x}SiR'NCO$, wherein x is an integer having a value of 0, 1, 2, or 3, each R separately represents an alkyl group of 1 to 12 carbon atoms, a halogenated alkyl group of 1 to 12 carbon atoms, a cycloalkyl group or a halogenated cycloalkyl group of 5 to 8 carbon atoms, an aryl group of 6 to 14 carbon atoms, or an alkaryl or aralkyl group of 7 to 15 carbon atoms, each R'' separately represents R, a silyl group R_3Si-, a siloxy group $R_3Si(OSiR_2)_m$- wherein m is an integer having a value of 1 to 4, or two R'' groups together may form a divalent siloxy group of the formula $-SiR_2(OSiR_2)_n$- wherein n is an integer having a value of 3, 4, or 5, and R is as defined above, and R' is a divalent hydrocarbon group of 1 to 20 carbon atoms attached to silicon by a silicon-carbon bond, and wherein R and R' optionally contain heteroatom functional groups selected from the group consisting of ether, thioether, sulfone, ketone, ester, amide, nitrile, or halogen.

3. The method of Claim 1 wherein the elevated temperature is between 300° C and 600° C and said reaction zone is maintained at a reduced pressure between $1{,}3 \cdot 10^3$ and $101{,}3 \cdot 10^3$ Pa (10 mm and 760 mm Hg).

4. The method of Claim 2 wherein R' is selected from the group consisting of divalent alkylene groups, divalent arylene groups, divalent alkarylene groups, and divalent aralkylene groups.

5. The method of Claim 2 wherein R is a methyl group or an ethyl group and the R goups attached to oxygen atoms are the same, x is 0 or 1, and R' is $-(C_nH_{2n})-$, where n is an integer of 3 to 6.

6. The method of Claim 1 wherein the carbamatoorganosilane is selected from the group consisting of $(MeO)_3Si(CH_2)_3NHCO_2Me$, $Me(MeO)_2Si(CH_2)_3NHCO_2Me$, and $(EtO)_3Si(CH_2)_3NHCO_2Et$ where Me is a methyl group and Et is an ethyl group.

7. The method of Claim 2 wherein the isocyanatoorganosilane is selected from the group consisting of $Me(Me_3SiO)_2Si(CH_2)_3NCO$, $(Me_3SiO)_3Si(CH_2)_3NCO$, $(OSiMe_2)_3OSiMe(CH_2)_3NCO$, and $(OSiMe_2)_4OSiMe(CH_2)_3NCO$, where Me is a methyl group.

8. The method of Claim 1 wherein the reaction zone comprises a continuous flow-through metal tube reactor with means for vaporizing said carbamatoorganosilane and for collecting said isocyanatoorganosilane.

9. An isocyanatoorganosilane having the formula $R_x(R''O)_{3-x}SiR'NCO$, wherein x is an integer having a value of 0, 1, 2, or 3, each R separately represents an alkyl group of 1 to 12 carbon atoms, a halogenated alkyl group of 1 to 12 carbon atoms, a cycloalkyl group or a halogenated cycloalkyl group of 5 to 8 carbon atoms, an aryl group of 6 to 14 carbon atoms, or an alkaryl or aralkyl group of 7 to 15 carbon atoms, each R'' separately represents R, a silyl group R_3Si-, a siloxy group $R_3Si(OSiR_2)_m$- wherein m is an integer having a value of 1 to 4, or two R'' groups together may form a divalent siloxy group of the formula $-SiR_2(OSiR_2)_n$- wherein n is an integer having a value of 3, 4, or 5, and R is as defined above, and R' is selected from the group consisting of $-CH_2CH_2CMe_2-$, $-CH_2CH_2CHMeCH_2-$, $-CH_2CH_2CMe_2CH_2-$, and $-CH_2CHMeCH_2-$, where Me is a methyl group.

Patentansprüche

1. Verfahren zur Herstellung eines Isocyanatorganosilans, umfassend das Verdampfen eines Carbamatorganosilans und das Erhitzen des verdampften Carbamatorganosilans in einer Reaktionszone bei einer erhöhten Temperatur für einen ausreichenden Zeitraum zur Bildung des Isocyanatorganosilans.

2. Verfahren gemäß Anpruch 1, worin das Isocyanatorganosilan die Formel $R_x(R"O)_{3-x}$ SiR'NCO hat, worin x eine ganze Zahl mit einem Wert von 0, 1, 2 oder 3 ist, jedes R gesondert für eine Alkylgruppe mit 1-12 Kohlenstoffatomen, eine halogenierte Alkylgruppe mit 1-12 Kohlenstoffatomen, eine Cycloalkylgruppe oder eine halogenierte Cycloalkylgruppe mit 5-8 Kohlenstoffatomen, eine Arylgruppe mit 6-14 Kohlenstoffatomen oder eine Alkaryl- oder Aralkylgruppe mit 7-15 Kohlenstoffatomen steht, jedes R" gesondert für R, eine Silylgruppe R_3Si-, eine Siloxylgruppe $R_3Si(OSiR_2)_m$- steht, worin m eine ganze Zahl mit einem Wert von 1-4 ist, oder zwei R"-Gruppen zusammen eine zweiwertige Siloxygruppe der Formel $SiR_2(OSiR_2)_n$- bilden können, worin n eine ganze Zahl mit einem Wert von 3, 4 oder 5 ist, und R wie oben definiert ist, und R' eine zweiwertige Kohlenwasserstoffgruppe mit 1-20 Kohlenstoffatomen, die an Silizium durch eine Silizium-Kohlenstoff-Bindung gebunden ist, ist, und worin R und R' gegebenenfalls funktionelle Heteroatomgruppen enthalten können, die gewählt sind aus der Gruppe, bestehend aus Ether, Thioether, Sulfon, Keton, Ester, Amid, Nitril oder Halogen.

3. Verfahren gemäß Anspruch 1, wobei die erhöhte Temperatur zwischen 300°C und 600°C liegt und die Reaktionszone bei einem verminderten Druck zwischen $1,3*10^3$ und $101,3*10^3$Pa (10mm und 760 mm Hg) gehalten wird.

4. Verfahren gemäß Anspruch 2, wobei R' aus der Gruppe gewählt wird, die aus zweiwertigen Alkylengruppen, zweiwertigen Arylengruppen, zweiwertigen Alkarylengruppen und zweiwertigen Aralkylengruppen besteht.

5. Verfahren gemäß Anspruch 2, wobei R eine Methylgruppe oder eine Ethylgruppe ist und 0 die R-Gruppen, die an Sauerstoffatomen gebunden sind, gleich sind, x 0 oder 1 ist und R' $-(C_nH_{2n})-$ ist, wenn n eine ganze Zahl von 3 - 6 ist.

6. Verfahren gemäß Anspruch 1, wobei das Carbamatorganosilan aus der Gruppe gewählt wird, die aus $(MeO)_3Si(CH_2)_3NHCO_2Me$, $Me(MeO)_2Si(CH_2)_3NHCO_2Me$ und $(EtO)_3Si(CH_2)_3NHCO_2Et$ besteht, wobei Me eine Methylgruppe ist und Et eine Ethylgruppe ist.

7. Verfahren gemäß Anspruch 2, wobei das Isocyanatorganosilan aus der Gruppe gewählt wird, welche aus $(Me_3SiO)_2Si(CH_2)_3NCO$, $(Me_3SiO)_3Si(CH_2)_3NCO$, $(OSiMe_2)_3OSiMe(CH_2)_3NCO$ und $(OSiMe_2)_4OSiMe(CH_2)_3NCO$ besteht, wobei Me eine Methylgruppe ist.

8. Verfahren gemäß Anspruch 1, wobei die Reaktionszone einen Metallrohrreaktor mit kontinuierlichem Durchfluß und mit Einrichtungen zur Verdampfung des Carbamatorganosilans und zur Sammlung des Isocyanatorganosilans umfaßt.

9. Isocyanatorganosilan die Formel $R_x(R"O)_{3-x}$ SiR'NCO hat, worin x eine ganze Zahl mit einem Wert von 0, 1, 2 oder 3 ist, jedes R gesondert für eine Alkylgruppe mit 1-12 Kohlenstoffatomen, eine halogenierte Alkylgruppe mit 1-12 Kohlenstoffatomen, eine Cycloalkylgruppe oder eine halogenierte Cycloalkylgruppe mit 5-8 Kohlenstoffatomen, eine Arylgruppe mit 6-14 Kohlenstoffatomen oder eine Alkaryl- oder Aralkylgruppe mit 7-15 Kohlenstoffatomen steht, jedes R" gesondert für R, eine Silylgruppe R_3Si-, eine Siloxylgruppe $R_3Si(OSiR_2)_m$-steht, worin m eine ganze Zahl mit einem Wert von 1-4 ist, oder zwei R"-Gruppen zusammen eine zweiwertige Siloxygruppe der Formel $-SiR_2(OSiR_2)_n$- bilden können, worin n eine ganze Zahl von 3, 4 oder 5 ist, und R wie oben definiert ist, und R' aus der Gruppe gewählt ist, die aus $-CH_2CH_2CMe_2-$, $-CH_2CH_2CHMeCH_2-$, $-CH_2CH_2CMe_2CH_2-$, und $-CH_2CHMeCH_2-$ besteht, wobei Me eine Methylgruppe ist.

Revendications

1. Procédé de production d'un isocyanato-organosilane, comprenant la vaporisation d'un carbamoto-organo-silane et le chauffage de ce carbamato-organosilane vaporisé dans une zone de réaction à une température élevée pendant une durée suffisante pour former cet isocyanato-organosilane.

2. Procédé suivant la revendication 1, dans lequel l'isocyanato-organosilane répond à la formule $R_x(R"O)_{3-x}SiR'NCO$, dans laquelle x est un nombre entier ayant la valeur 0, 1, 2 ou 3, chaque R représente séparément un groupe alkyle de 1 à 12 atomes de carbone, un groupe alkyle halogéné de 1 à 12 atomes de carbone, un groupe cycloalkyle ou un groupe cycloalkyle halogéné de 5 à 8 atomes de carbone, un groupe aryle de 6 à 14 atomes de carbone ou un groupe alkaryle ou aralkyle de 7 à 15 atomes de carbone, chaque R" représente séparément R, un groupe silyle R_3Si-, un groupe siloxy $R_3Si(OSiR_2)_m$- dans lequel m est un nombre entier ayant une valeur de 1 à 4, ou bien deux groupes R" peuvent former ensemble un groupe siloxy divalent de formule $-SiR_2(OSiR_2)_n$- dans laquelle n est un nombre entier ayant la valeur 3, 4 ou 5, et R est tel que défini ci-dessus, et R' est un groupe hydrocarbyle

divalent de 1 à 20 atomes de carbone lié au silicium par une liaison silicium-carbone, et où R et R' comportent facultativement des groupes fonctionnels contenant un hétéroatome, choisis dans le groupe consistant en éther, thioéther, sulfone, cétone, ester, amide, nitrile ou un halogène.

3. Procédé suivant la revendication 1, dans lequel la température élevée se situe entre 300°C et 600°C et la zone de réaction est maintenue sous une pression réduite comprise entre $1,3.10^3$ et $101,3.10^3$ Pa (10 mm et 760 mm de Hg).

4. Procédé suivant la revendication 2, dans lequel R' est choisi entre des groupes alkylène divalents, des groupes aryléne divalents, des groupes alkarylène divalents et des groupes aralkylène divalents.

5. Procédé suivant la revendication 2, dans lequel R est un groupe méthyle ou un groupe éthyle et les groupes R liés à des atomes d'oxygène sont les mêmes, x a la valeur 0 ou 1 et R' est un groupe $-(C_nH_{2n})-$, dans lequel n est un nombre entier de 3 à 6.

6. Procédé suivant la revendication 1, dans lequel le carbamato-organosilane est choisi dans le groupe consistant en $(MeO)_3Si(CH_2)_3NHCO_2Me$, $Me(MeO)_2Si(CH_2)_3NHCO_2Me$ et $(EtO)_3Si(CH_2)_3NHCO_2Et$, où Me est un groupe méthyle et Et est un groupe éthyle.

7. Procédé suivant la revendication 2, dans lequel l'isocyanato-organosilane est choisi dans le groupe consistant en $Me(Me_3SiO)_2Si(CH_2)_3NCO$, $(Me_3SiO)_3Si(CH_2)_3NCO$, $(OSiMe_2)_3OSiMe(CH_2)_3NCO$ et $(OSiMe_2)_4OSiMe(CH_2)_3NCO$, où Me est un groupe méthyle.

8. Procédé suivant la revendication 1, dans lequel la zone de réaction comprend un réacteur à tube métallique à écoulement continu équipé de moyens permettant de vaporiser le carbamato-organosilane et de recueillir l'isocyanato-organosilane en question.

9. Isocyanato-organosilane répondant à la formule $R_x(R"O)_{3-x}SiR'NCO$, dans laquelle x est un nombre entier ayant la valeur 0, 1, 2 ou 3, chaque R représente séparément un groupe alkyle de 1 à 12 atomes de carbone, un groupe alkyle halogéné de 1 à 12 atomes de carbone, un groupe cycloalkyle ou un groupe cycloalkyle halogéné de 5 à 8 atomes de carbone, un groupe aryle de 6 à 14 atomes de carbone ou un groupe alkaryle ou aralkyle de 7 à 15 atomes de carbone, chaque R" représente séparément R, un groupe silyle R_3Si-, un groupe siloxy $R_3Si(OSiR_2)_m-$ dans lequel m est un nombre entier ayant une valeur de 1 à 4, ou bien deux groupes R" peuvent former ensemble un groupe siloxy divalent de formule $-SiR_2(OSiR_2)_n-$ dans laquelle n est un nombre entier ayant la valeur 3, 4 ou 5, et R est tel que défini ci-dessus, et R' est choisi dans le groupe consistant en $-CH_2CH_2CMe_2-$, $-CH_2CH_2CHMeCH_2-$, $-CH_2CH_2CMe_2CH_2-$ et $-CH_2CHMeCH_2-$, où Me est un groupe méthyle.

C. Oliver Kappe, Alexander Stadler

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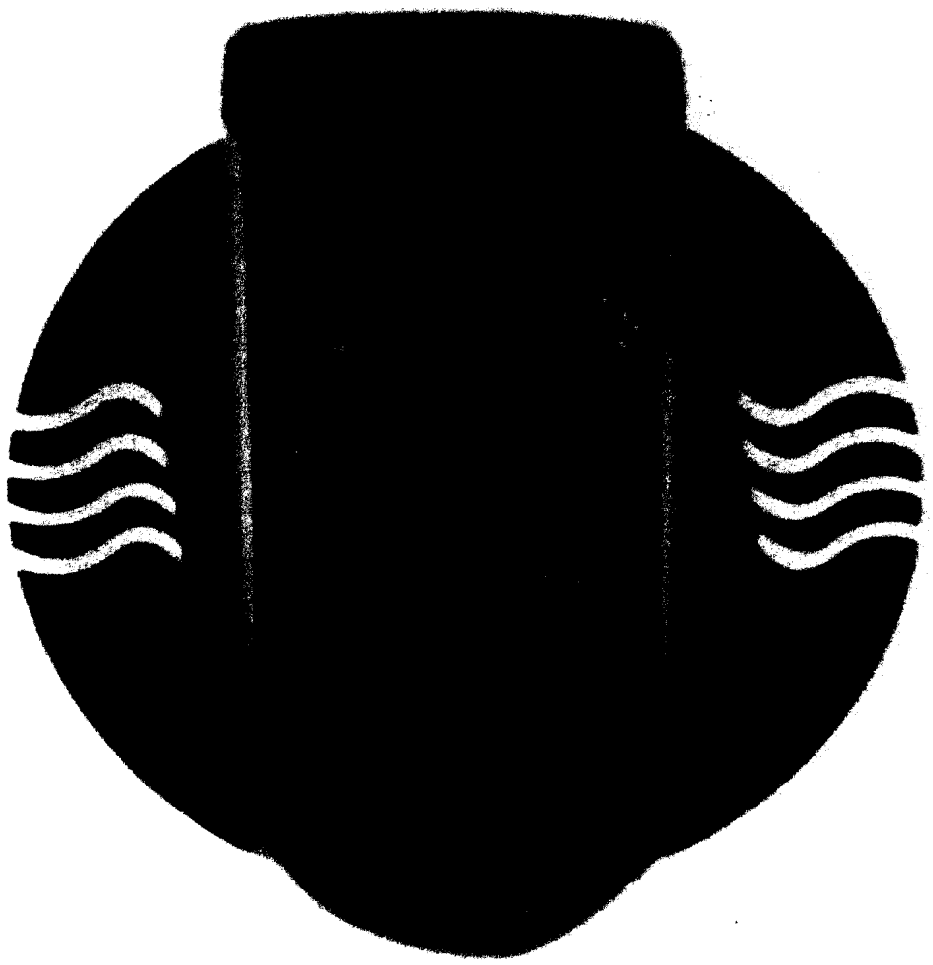
Microwaves in Organic and Medicinal Chemistry



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Series Editors:
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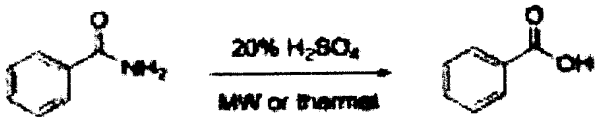
G. Folkers

to a reaction vessel in a focused manner. The Bunsen burner was later superseded by the isomantle, the oil bath or the hot plate as a means of applying heat to a chemical reaction. In the past few years, heating and driving chemical reactions by microwave energy has been an increasingly popular theme in the scientific community [1, 2].

Microwave energy, originally applied for heating foodstuffs by Percy Spencer in the 1940s, has found a variety of technical applications in the chemical and related industries since the 1950s, in particular in the food-processing, drying, and polymer industries. Other applications range from analytical chemistry (microwave digestion, ashing, extraction) [3] to biochemistry (protein hydrolysis, sterilization) [3], pathology (histoprocessing, tissue fixation) [4], and medical treatments (diathermy) [5]. Somewhat surprisingly, microwave heating has only been implemented in organic synthesis since the mid-1980s. The first reports on the use of microwave heating to accelerate organic chemical transformations (MAOS) were published by the groups of Richard Gedye (Scheme 1.1) [6] and Raymond J. Giguere/George Majetich [7] in 1986. In those early days, experiments were typically carried out in sealed Teflon or glass vessels in a domestic household microwave oven without any temperature or pressure measurements. The results were often violent explosions due to the rapid uncontrolled heating of organic solvents under closed-vessel conditions. In the 1990s, several groups started to experiment with solvent-free microwave chemistry (so-called dry-media reactions), which eliminated the danger of explosions [8]. Here, the reagents were pre-adsorbed onto either an essentially microwave-transparent (i.e., silica, alumina or clay) or strongly absorbing (i.e., graphite) inorganic support, that additionally may have been doped with a catalyst or reagent. Particularly in the early days of MAOS, the solvent-free approach was very popular since it allowed the safe use of domestic microwave ovens and standard open-vessel technology. While a large number of interesting transformations using "dry-media" reactions have been published in the literature [8], technical difficulties relating to non-uniform heating, mixing, and the precise determination of the reaction temperature remained unresolved, in particular when scale-up issues needed to be addressed.



thermal: 1 h, 90 % yield (reflux)
MW: 10 min, 99 % yield (sealed vessel)

Scheme 1.1 Hydrolysis of benzamide. The first published example (1986) of microwave-assisted organic synthesis.

Alternatively, microwave-assisted synthesis has been carried out using standard organic solvents under open-vessel conditions. If solvents are heated by microwave irradiation at atmospheric pressure in an open vessel, the boiling point of the solvent typically limits the reaction temperature that can be achieved. In order to nonre-

theless achieve high reaction rates, high-boiling microwave-absorbing solvents have been frequently used in open-vessel microwave synthesis [9]. However, the use of these solvents presented serious challenges in relation to product isolation and recycling of the solvent. Because of the recent availability of modern microwave reactors with on-line monitoring of both temperature and pressure, MAOS in dedicated sealed vessels using standard solvents – a technique pioneered by Christopher R. Strauss in the mid-1990s [10] – has been celebrating a comeback in recent years. This is clearly evident surveying the recently published (since 2001) literature in the area of controlled microwave-assisted organic synthesis (MAOS). It appears that the combination of rapid heating by microwaves with sealed-vessel (autoclave) technology will most likely be the method of choice for performing MAOS on a laboratory scale in the future. Importantly, recent innovations in microwave reactor technology now allow controlled parallel and automated sequential processing under sealed-vessel conditions, and the use of continuous- or stop-flow reactors for scale-up purposes.

Since the early days of microwave synthesis, the observed rate accelerations and sometimes altered product distributions compared to oil-bath experiments have led to speculation on the existence of so-called "specific" or "non-thermal" microwave effects [11]. Historically, such effects were claimed when the outcome of a synthesis performed under microwave conditions was different from that of the conventionally heated counterpart at the same apparent temperature. Reviewing the present literature [12], it appears that today most scientists agree that in the majority of cases the reason for the observed rate enhancements is a purely thermal/kinetic effect, i.e., a consequence of the high reaction temperatures that can rapidly be attained when irradiating polar materials in a microwave field, although effects that are caused by the unique nature of the microwave dielectric heating mechanism ("specific microwave effects") clearly also need to be considered. While for the medicinal chemist in industry this discussion may seem largely irrelevant, the debate on "microwave effects" is undoubtedly going to continue for many years in the academic world. Regardless of the nature of the observed rate enhancements (for further details on microwave effects, see Section 2.5), microwave synthesis has now truly matured and has moved from a laboratory curiosity in the late 1980s to an established technique in organic synthesis, heavily used in both academia and industry.

The initially slow uptake of the technology in the late 1980s and 1990s has been attributed to its lack of controllability and reproducibility, coupled with a general lack of understanding of the basics of microwave dielectric heating. The risks associated with the flammability of organic solvents in a microwave field and the lack of available dedicated microwave reactors allowing for adequate temperature and pressure control were major concerns. Important instrument innovations (see Chapter 3) now allow for careful control of time, temperature, and pressure profiles, paving the way for reproducible protocol development, scale-up, and transfer from laboratory to laboratory and from scientist to scientist. Today, microwave chemistry is as reliable as the vast arsenal of synthetic methods that preceded it. Since 2001, therefore, the number of publications related to MAOS has increased dramatically (Fig. 1.1), to such a level that it might be assumed that, in a few years, most chemists

um and electrical energy is converted into kinetic or thermal energy, and ultimately into heat. It should be emphasized that the interaction between microwave radiation and the polar solvent which occurs when the frequency of the radiation approximately matches the frequency of the rotational relaxation process is not a quantum mechanical resonance phenomenon. Transitions between quantized rotational bands are not involved and the energy transfer is not a property of a specific molecule, but the result of a collective phenomenon involving the bulk [4, 5]. The heat is generated by frictional forces occurring between the polar molecules, the rotational velocity of which has been increased by the coupling with the microwave irradiation. It should also be noted that gases cannot be heated under microwave irradiation, since the distance between the rotating molecules is too great. Similarly, ice is also (nearly) microwave transparent, since the water dipoles are constrained in a crystal lattice and cannot move as freely as in the liquid state.

The second major heating mechanism is the ionic conduction mechanism (Fig. 2.3.b) [4, 5]. During ionic conduction, as the dissolved charged particles in a sample (usually ions) oscillate back and forth under the influence of the microwave field, they collide with their neighboring molecules or atoms. These collisions cause agitation or motion, creating heat. Thus, if two samples containing equal amounts of distilled water and tap water, respectively, are heated by microwave irradiation at a fixed radiation power, more rapid heating will occur for the tap water sample due to its ionic content. Such ionic conduction effects are particularly important when considering the heating behavior of ionic liquids in a microwave field (see Section 4.3.3.2). The conductivity principle is a much stronger effect than the dipolar rotation mechanism with regard to the heat-generating capacity.

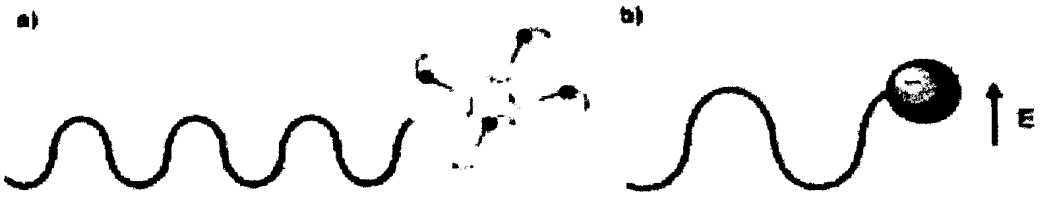


Fig. 2.3 (a) Dipolar polarization mechanism. (b) Dipolar molecules try to align with an oscillating electric field. Ionic conduction mechanism. Ions in solution will move in the electric field.

2.3 Dielectric Properties

The heating characteristics of a particular material (for example, a solvent) under microwave irradiation conditions are dependent on the dielectric properties of the material. The ability of a specific substance to convert electromagnetic energy into heat at a given frequency and temperature is determined by the so-called loss tangent, $\tan\delta$. The loss factor is expressed as the quotient $\tan\delta = \varepsilon''/\varepsilon'$, where ε'' is the dielectric loss, indicative of the efficiency with which electromagnetic radiation is

THE USE OF MICROWAVE HEATING TO PROMOTE ORGANIC REACTIONS

G. Majetich and R. Hicks

This study documents the usefulness of microwave heating for the preparation of a wide variety of organic compounds using a commercial microwave system equipped with a built-in pressure unit and an external temperature monitoring device. The results of control experiments conducted under conventional heating conditions are also provided for each reaction. Most of the reactions studied showed drastically reduced reaction times compared with conventional heating, due to the higher temperatures attained. These results show that microwave heating is useful for preparative organic chemistry.

Key Words:
Diels-Alder reactions, *ortho*-Claisen rearrangements, ene reactions, Conversion of alcohols into alkyl bromides, Finkelstein reactions, Oxidations, Esterifications, Hydrolyses, Williamson ether syntheses, and Aryl ether cleavages.

ABOUT THE AUTHORS:
George Majetich and Rodgers Hicks are affiliated with the Department of Chemistry, The University of Georgia, Athens, Georgia 30602.

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As early as 1975, there were reports of increased reaction rates for the acid dissolution of samples heated with microwaves [Abu-Samra et al., 1975]. Shortly thereafter, this technology evolved into microwave heating of chemical reactions in sealed containers. Our early studies [Giguere et al., 1986 and 1987] and those of Gedye and coworkers [Gedye et al., 1986; 1988] showed that microwave-promoted reactions occur with a dramatic decrease in reaction time. In some cases, cleaner reactions with easier workups were observed compared with conventional heating. These findings stimulated the study of microwave heating by ourselves and others, and advances in the field are summarized in several reviews [Abramovitch, 1991; Mingos and Baghurst, 1991; Majetich and Wheless, 1995]. In this article we report the results of a survey of common organic reactions: Diels-Alder reactions, *ortho*-Claisen rearrangements, ene reactions, the conversion of alcohols into alkyl bromides, Finkelstein reactions, oxidations, esterifications, hydrolyses, Williamson ether syntheses, and aryl ether cleavages. Conventional reaction conditions for each of the reactions studied were optimized before making comparisons with the microwave results. Hence, many reactions previously thought to require lengthy heating periods, thereby making them ideal candidates for our study, were shown, after optimization, to either be rapid transformations or not require extensive heating.

Materials and Methods

All of the reactions described were carried out using a CEM Model MDS-81D oven equipped with a pressure monitoring device and a MetriCorp fiberoptics temperature monitoring device. The magnetron tube supplies 630 watts (± 70 watts). Effective power levels of 0-100% of this value are available as a train of timed pulses. The MDS-81D unit is designed so that irradiation stops when a predetermined pressure is reached; thus, the pressure monitor functions as a baristat and controls the reaction temperature indirectly. Some changes in temperature were noted in reactions conducted at constant pressure — we attribute these fluctuations to changes in the reaction mixture composition and its volatility.

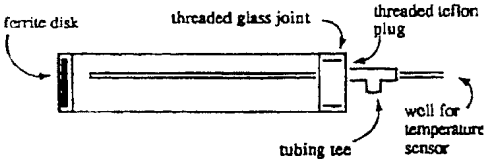
Most of the experiments were performed in sealed Teflon [poly(tetrafluoro-ethylene)] acid digestion vessels. These Teflon containers can be used at up to fourteen atmospheres of pressure (200 psi). They are resistant to most of the chemi-

Evidence Appendix 5

vals used in this study; however, at temperatures greater than 250°C, these digestion vessels deform, often with vessel rupture. For microwave-promoted organic reactions in open vessels under atmospheric pressure, see Bose et al. [1990].

The solvents used in our study include dimethylformamide (DMF), water, 2-butanone, methanol, and ethanol — all of which couple efficiently with microwaves. DMF is our solvent of choice for two reasons: first, it is a very efficient coupler of microwaves allowing high reaction temperatures to be reached, and secondly, DMF is miscible with water. Upon completion of the reaction, the DMF is removed by adding water to the reaction mixture followed by standard ethereal workup. On occasion, cosolvents were added to allow the pressure monitoring system to function. For example, in the olefin isomerization (Miscellaneous Reactions), the vapor pressure of dimethyl sulfoxide (DMSO) was too low to engage the pressure monitoring unit; adding ethanol as a cosolvent, which is more volatile than DMSO, overcame this problem without complicating the reaction.

Nonpolar solvents, such as hexanes, carbon tetrachloride, diethyl ether or benzene, do not absorb or couple with microwaves and therefore are generally not useful. In a few cases, the use of nonpolar solvents was unavoidable. In these cases a custom quartz vessel (Figure 1) containing a ferrite disk was employed. Ferrite readily absorbs microwave energy and gives up heat to the reaction mixture through conduction, which provides heat indirectly to the reaction.



The body, including the chamber enclosing the heat source, is of quartz glass. The pressure monitor is connected to the sidearm of the tubing tee. The branch of the tee connected to the vessel is bored to ensure that pressure reaches the sidearm.

FIGURE 1: Custom vessel for heating reaction mixtures that do not couple with microwaves efficiently.

Finally, although effort was made to precisely measure the reaction times, temperatures, and pressures, the experimental conditions reported herein were optimized solely based on reaction yields.

Results and Discussions

Since this journal is interdisciplinary in nature, a brief description has been provided for each class of reaction studied.

Diels-Alder Reactions

Conjugated dienes undergo a cycloaddition reaction with certain multiple bonds to form cyclohexene rings. This process, named the Diels-Alder reaction after its two discoverers, is a powerful synthetic method because two carbon–carbon bonds are formed in a single step to give a functionalized cyclohexene ring. The reaction is most facile when the diene double bonds are electron-rich and the reacting multiple bond of the second component, called the dienophile, is electron-poor. Alkyl groups, aryl groups, and heteroatoms bearing electron pairs are electron-donating and will increase the reactivity of dienes to which they are attached. Atoms bearing either a full or partial positive charge, such as the carbon atom of a carbonyl group, have an electron-withdrawing effect and when directly attached to a dienophile they increase its reactivity.

Diels-Alder reactions involving nonactivated dienophiles typically require heating to temperatures above 300°C. Since the Teflon vessels in the MDS-81D system cannot withstand these temperatures, we selected only Diels-Alder reactions with activated dienophiles for our study. The results are summarized in Table 1.

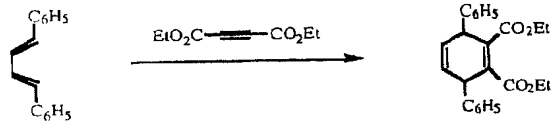
In the first example, the reaction is sluggish due to the steric bulk of the phenyl groups on 1,4-diphenyl-1,3-butadiene even though the dienophile is activated by the electron-withdrawing effects of two esters. The six hour reaction time was reduced by a factor of eighteen under microwave heating conditions, although there was a modest reduction in yield.

In the second example, the absence of steric hindrance in furan makes this reaction more facile than the previous one. The low boiling point of furan (32°C) necessitates that this reaction be done in a sealed vessel to prevent escape of the volatile reactant. This is inconvenient and entails the risk of explosion under conventional conditions. One advantage of the microwave system is the avoidance of these difficulties.

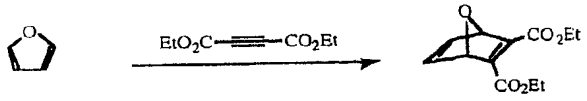
The reactions of anthracene with maleic anhydride (entry 3) and dimethyl fumarate (entry 4) are classic examples of the Diels-Alder reaction. In both cases a dramatic rate enhancement is observed with microwave heating and yields are comparable to those obtained by conventional methods.

Entry 5 shows a hetero-Diels-Alder reaction in which an atom other than carbon is incorporated into the new ring. Although simple ketones do not usually undergo this kind of reaction, the carbonyl group of diethyl oxomalonate is especially electron-poor because of the two ester groups attached to it. Two regioisomers are hypothetically possible from this reaction, but only one product is observed due to steric effects. The rate enhancement under microwave heating in this reaction is modest .

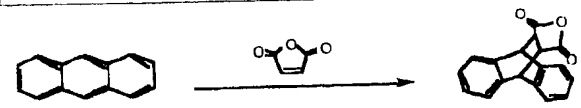
TABLE 1
Diels-Alder Reactions



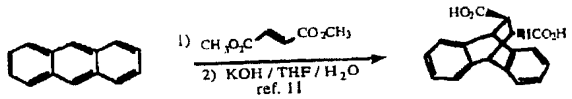
(1)	Conventional	Microwave
Solvent:	DMF	DMF
Reaction Temperature:	reflux (153°C)	198°→194°C (30 psi)
Yield:	67%	58%
Reaction Time:	6 hours	20 minutes



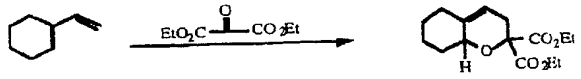
(2)	Conventional	Microwave
Solvent:	DMF	DMF
Reaction Temperature:	175°C(sealed tube)	163°→147°C(30 psi)
Yield:	68%	86%
Reaction Time:	15 minutes	10 minutes



(3)	Conventional	Microwave
Solvent:	DMF	DMF
Reaction Temperature:	reflux (153°C)	190°C (15 psi)
Yield:	86%	84%
Reaction Time:	45 minutes	4 minutes



(4)	Conventional	Microwave
Solvent:	DMF	DMF
Reaction Temperature:	reflux (153°C)	197°→192°C (20 psi)
Yield:	82%	75%
Reaction Time:	120 minutes	12 minutes



(5)	Conventional	Microwave
Solvent:	DMF	DMF
Reaction Temperature:	reflux (153°C)	198°→192°C (23 psi)
Yield:	55%	57%
Reaction Time:	60 minutes	30 minutes

ortho-Claisen Rearrangements

Three important sigmatropic reactions, the Cope rearrangement of a 1,5-diene, the Claisen rearrangement of an allyl vinyl ether, and the *ortho*-Claisen rearrangement of an allyl aryl ether, are depicted in Figure 2. These reactions, along with the Diels-Alder and ene reactions, are examples of pericyclic reactions — processes that involve concerted bond-making and breaking. Cope and Claisen rearrangements are single-step processes. *ortho*-Claisen rearrangements involve the initial pericyclic reaction followed by a tautomerization to restore aromaticity in the product.

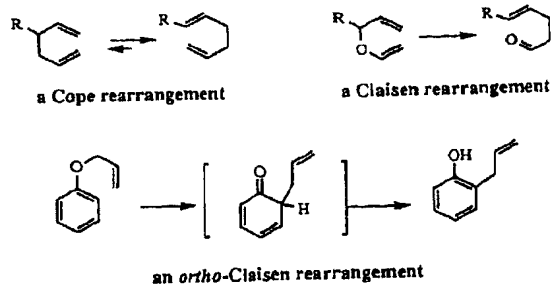


FIGURE 2: *Three Pericyclic Rearrangements.*

The elevated temperatures required (> 190 °C) in the three examples shown in Table 2 were easily achieved using DMF as the solvent. Entry 8 shows a *para*-Claisen rearrangement, in which the allyl unit migrates to the *para* position of the ring through a tandem *ortho*-Claisen / Cope rearrangement process (Figure 3).

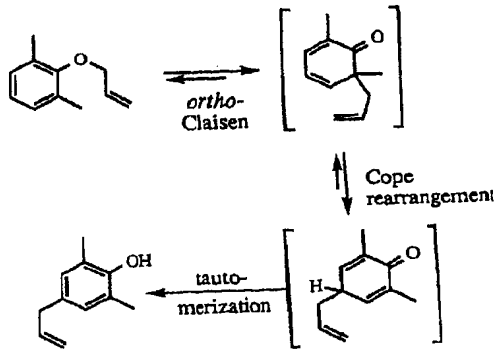


FIGURE 3: *Mechanism of the* para*-Claisen rearrangement.*

Ene Reactions

The "ene reaction" is a reaction of an alkene with an enophile (analogous to the Diels-Alder reaction of a diene with a dienophile) in which a single new carbon — carbon bond is formed and the position of the original double bond shifts through a cyclic transition state.

As in the Diels-Alder reaction, electron-rich enes and electron-poor enophiles are the most reactive. Reactions of enophiles not activated by electron-withdrawing groups usually require temperatures exceeding 300°C, so we selected only those reactions which proceed at temperatures safely attainable in the Teflon vessels. The results are given in Table 3.

Intramolecular reactions are entropically favored over the corresponding intermolecular cases, especially when a five- or six-membered ring is generated. The intramolecular cyclization shown in Entry 9 requires a high temperature because of the unactivated enophile (the triple bond). In contrast, in Entry 10 an activated enophile was employed; even though this reaction requires only twenty minutes under the conventional conditions, a significant rate enhancement is observed using microwave heating.

We also investigated examples of the Alder-Bong reaction [Giguere et al, 1987] which involves an ene reaction followed by an intramolecular Diels-Alder reaction to form interesting polycyclic systems (Figure 4). The intramolecular Diels-Alder step occurs rapidly and thus the intermediate formed by the initial ene reaction is not isolable.

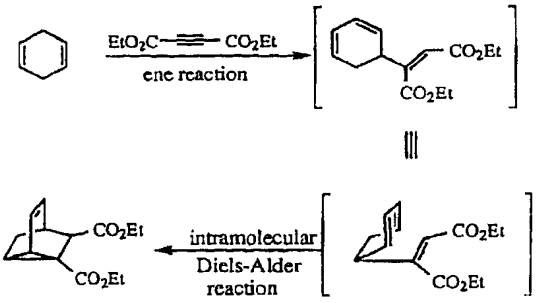


FIGURE 4: Mechanism of the Alder-Bong Reaction.

Three examples of the Alder-Bong reaction are reported. In Entry 11, the simplest case, a 120-fold rate enhancement by using microwave heating was observed. Furthermore, decomposition of the reactants, which contributes to the low yield under conventional reflux conditions, was greatly reduced by the shorter reaction time.

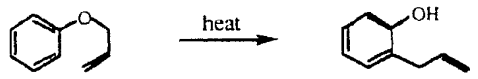
The two double bonds of the ene component in Entry 12 are not equivalent, hence two products are possible. The tetrasubstituted double bond is the more electron-rich, and the ene reaction at this bond leads to the formation of the major product 12a. The alternative ene reaction at the disubstituted double bond results in the formation of 12b. The higher yields for this reaction, compared to Entry 11, are attributed to the enhanced reactivity of the ene component which makes the initial ene reaction more favorable than decomposition.

Although two products are also possible in the reaction presented in Entry 13, only one product is formed.

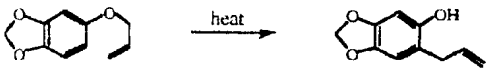
Conversion of Alcohols to Alkyl Bromides

The simplest and most common method for preparing an alkyl halide is to treat an alcohol with a mineral acid. The reaction

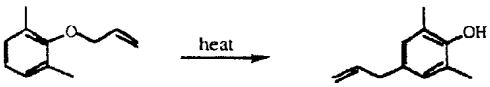
TABLE 2



(6)	*Conventional*	*Microwave*
Solvent:	DMF	DMF
Reaction Temperature:	reflux (153°C)	198°→193°C (30 psi)
Yield:	34%	80%
Reaction Time:	80 hours	5 hours

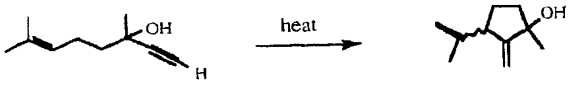


(7)	*Conventional*	*Microwave*
Solvent:	DMF	DMF
Reaction Temperature:	reflux (153°C)	195°C (30 psi)
Yield:	72%	97%
Reaction Time:	36 hours	5 minutes

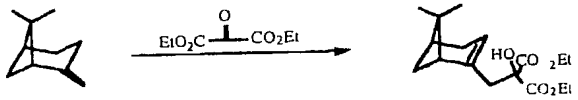


(8)	*Conventional*	*Microwave*
Solvent:	DMF	DMF
Reaction Temperature:	reflux (153°C)	197°→192°C (17 psi)
Yield:	83%	91%
Reaction Time:	4 days	20 minutes

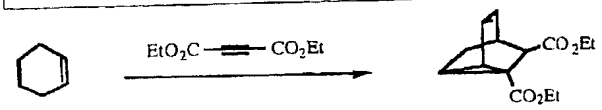
TABLE 3
Ene and Alder-Bong Reactions.



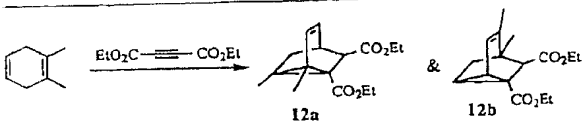
(9) *Conventional*	*Microwave*
Solvent: DMF	DMF
Reaction Temperature: reflux (153°C)	198°→196°C (23 psi)
Yield: 33%	73%
Reaction Time: 4 days	8 hours



(10) *Conventional*	*Microwave*
Solvent: DMF	DMF
Reaction Temperature: reflux (153°C)	199°C (20 psi)
Yield: 68%	71%
Reaction Time: 20 minutes	1 minute

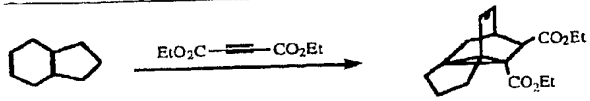


(11) *Conventional*	*Microwave*
Solvent: DMF	DMF
Reaction Temperature: reflux (153°C)	184°→179°C (90 psi)
Yield: 14%	49%
Reaction Time: 40 hours	20 minutes



12a **12b**

(12) *Conventional*	*Microwave*
Solvent: DMF	DMF
Reaction Temperature: reflux (153°C)	183°→180°C (30 psi)
Yield: 24% of **12a**; 5% of **12b**	78% of **12a**; 17% of **12b**
Reaction Time: 5 hours	20 minutes

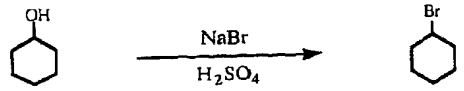


(13) *Conventional*	*Microwave*
Solvent: DMF	DMF
Reaction Temperature: reflux (153°C)	182°→178°C (15 psi)
Yield: 41%	69%
Reaction Time: 5 hours	20 minutes

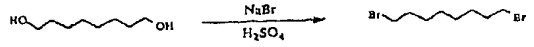
of a mineral acid with a tertiary alcohol is so rapid that it is normally carried out by bubbling gaseous mineral acid into a cold solution of the alcohol. Since these reactions are often complete within a few minutes, we did not expect the reactions of tertiary alcohols to benefit from microwave heating. In contrast, the conversion of a primary or a secondary alcohol into an alkyl halide requires both higher reaction temperatures and longer reaction times, and these reactions should benefit from microwave heating. Indeed, the three transformations shown in Table 4 occur in only a few minutes using microwave procedures.

While control conditions indicated that thirty minutes were required to completely convert cyclohexanol to cyclohexyl bromide, this transformation occurs rapidly using microwave heating (Entry 15). Moreover, gas chromatography (GC) analysis has indicated that this reaction proceeds by first dehydration of the alcohol to produce

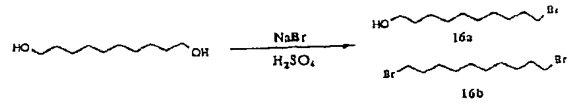
TABLE 4
Conversion of Alcohols to Alkyl Bromides.



(14) *Conventional*	*Microwave*
Solvent: water	water
Reaction Temperature: reflux (118°C)	137°→140°C (10 psi)
Yield: 33%	49%
Reaction Time: 30 minutes	10 minutes



(15) *Conventional*	*Microwave*
Solvent: water	water
Reaction Temperature: reflux (118°C)	158°C (15 psi)
Yield: 70%	60%
Reaction Time: 20 minutes	30 seconds



(16) *Conventional*	*Microwave*
Solvent: water	water
Reaction Temperature: reflux (118°C)	156°→158°C (15 psi)
Yield: 23% of **16a**; 3% of **16b**	37% of **16a**; 24% of **16b**
Reaction Time: 30 minutes	30 seconds

cyclohexene, which then reacts with HBr to produce cyclohexyl bromide. This addition reaction involves a carbocation intermediate which can undergo polymerization and other side reactions resulting in low yields. Under microwave heating, the shorter reaction time minimizes these losses.

1,8-Octanediol (entry 15) is easily converted to the dibromide under both microwave and conventional conditions. The bromination of the homologous ten-carbon diol (Entry 16), however, is quite slow under conventional heating conditions due to the low solubility of the initial halohydrin product (cf. 16a) in the aqueous acid solvent system. Under microwave heating, dibromide 16b is obtained quickly. Here, which product is desired will influence the choice of heating method.

Finkelstein Reactions

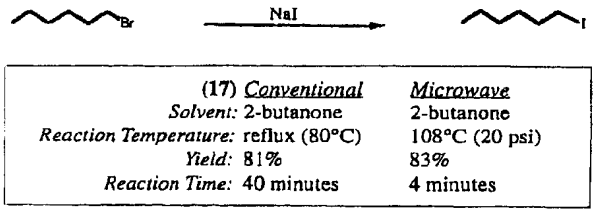
The classic Finkelstein procedure, a nucleophilic substitution reaction, is an equilibrium process. Alkyl iodides are prepared from alkyl chlorides by taking advantage of the fact that sodium chloride is insoluble in acetone. Thus, when an alkyl chloride or alkyl bromide is treated with sodium iodide in acetone to give an alkyl iodide, sodium chloride or sodium bromide precipitates out of the reaction mixture shifting the equilibrium in favor of alkyl iodide formation (Table 5). In our microwave experiments, we used 2-butanone rather than acetone as a solvent because its boiling point (80°C) is higher than that of acetone (56°C) and the higher temperatures result in shorter reaction times. The first two examples in Table 5 involve unhindered primary alkyl bromides and the advantage of microwave heating is modest. The reaction with the more hindered cyclohexyl bromide is extremely slow under reflux conditions but can be accomplished in a reasonable time using the microwave system.

Oxidations

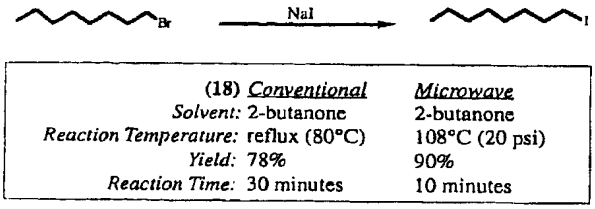
A common reaction of alcohols is their oxidation to produce carbonyl-containing compounds. Oxidation of primary alcohols gives aldehydes or carboxylic acids depending on the oxidant used, while secondary alcohols yield ketones. Tertiary alcohols do not react except under extremely vigorous conditions.

While most oxidations occur easily at ambient or low temperatures and would not benefit from microwave heating, we found that manganese dioxide oxidations are applicable to this new technology. Manganese dioxide is a mild oxidant which selectively oxidizes allylic and benzylic alcohols. A large excess of manganese dioxide is required for these oxidations as well as lengthy reaction times. Diethyl ether, the solvent of choice, does not efficiently absorb microwave radiation, so we carried out our microwave studies on these reactions in a quartz reaction vessel heated by a piece of ferrite (cf. Figure 1). In the three examples in Table 6, using microwave heating proved vastly superior for the oxidation in terms of both yield and reaction time. Each of these reactions is very clean, and although none go to completion regardless of heating period, the unreacted substrates can be recovered and recycled.

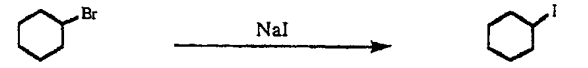
TABLE 5



(17) *Conventional*	*Microwave*
Solvent: 2-butanone	2-butanone
Reaction Temperature: reflux (80°C)	108°C (20 psi)
Yield: 81%	83%
Reaction Time: 40 minutes	4 minutes



(18) *Conventional*	*Microwave*
Solvent: 2-butanone	2-butanone
Reaction Temperature: reflux (80°C)	108°C (20 psi)
Yield: 78%	90%
Reaction Time: 30 minutes	10 minutes



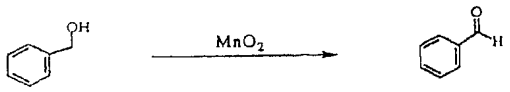
(19) *Conventional*	*Microwave*
Solvent: 2-butanone	2-butanone
Reaction Temperature: reflux (80°C)	131°→129°C (20 psi)
Yield: 80%	72%
Reaction Time: 80 hours	4 hours

Esterifications

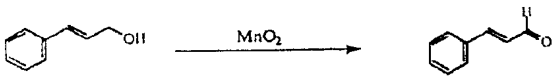
One important reaction of carboxylic acids is their conversion into esters. Although there are many procedures for accomplishing this transformation, the simplest method was discovered in 1895 by Fischer and Speier, wherein a carboxylic acid and an alcohol condense in the presence of a mineral acid catalyst. The need to use excess alcohol as solvent limits this method to the synthesis of simple esters; three examples are given in Table 7.

The esterification of benzoic acid requires over an hour of reflux, dramatically reduced to only one minute under microwave heating. The lengthy reaction time required for the

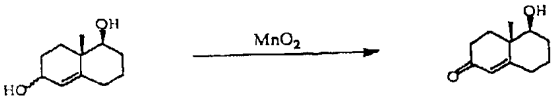
TABLE 6
Oxidations



(20)	*Conventional*	*Microwave*
Solvent:	diethyl ether	diethyl ether
Reaction Temperature:	reflux (36°C)	104°C (90 psi)
Yield:	20%	52%
Reaction Time:	8 hours	7 minutes

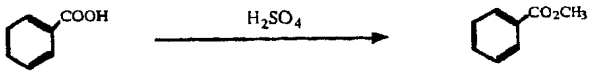


(21)	*Conventional*	*Microwave*
Solvent:	diethyl ether	diethyl ether
Reaction Temperature:	reflux (36°C)	116°C (90 psi)
Yield:	44%	82%
Reaction Time:	5 hours	3 minutes

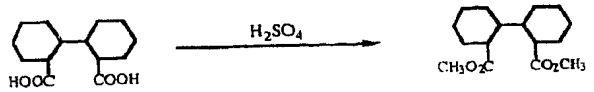


(22)	*Conventional*	*Microwave*
Solvent:	diethyl ether	diethyl ether
Reaction Temperature:	reflux (36°C)	103°C (90 psi)
Yield:	33%	79%
Reaction Time:	90 minutes	7 minutes

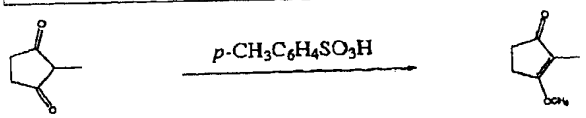
TABLE 7
Fischer Esterifications



(23)	*Conventional*	*Microwave*
Solvent:	methanol	methanol
Reaction Temperature:	reflux (65°C)	120°C (50 psi)
Yield:	92%	92%
Reaction Time:	80 minutes	1 minute



(24)	*Conventional*	*Microwave*
Solvent:	methanol	methanol
Reaction Temperature:	reflux (65°C)	118°→108°C (70 psi)
Yield:	80%	72%
Reaction Time:	80 hours	4 hours



(25)	*Conventional*	*Microwave*
Solvent:	methanol	methanol
Reaction Temperature:	reflux (65°C)	132°→136°C (90 psi)
Yield:	84%	86%
Reaction Time:	90 minutes	2 minutes

esterification shown in Entry 24 is because of the insolubility of the diacid in methanol. In this case much of the rate enhancement under microwave heating is probably due to increased solubility of the diacid at the higher reaction temperature.

Finally, the conversion of 2-methylcyclopentane-1,3-dione to 3-methoxy-2-methylcyclopentenone (Entry 25) is included as an esterification because a vinylogous ester is produced.

Hydrolyses

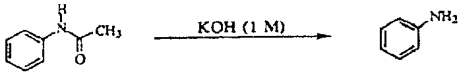
Esters, amides, and nitriles are hydrolyzed either by aqueous acid or aqueous base to the carboxylic acid and the corresponding alcohol or amine. The extensive heating usually required make these reactions ideal candidates for the application of microwave technology. All of these processes (Table 8) were efficiently achieved with dramatic rate enhancements using microwave heating. Note also the improved selectivity in the hydrolysis of 2-methylbenzonitrile (Entry 28). The initial product is amide 28b, which further hydrolyzes to the carboxylic acid. The amide product is obtained more selectively at the higher temperature due to greater rate enhancement of the first step.

The effect of steric hindrance on hydrolysis is clearly evident in the peptide hydrolyses studied. The isobutyl side chain of leucine makes glycyl-*d,l*-leucine as resistant to hydrolysis as unhindered glycyl-glycyl-glycine. Entry 31 shows the unreasonable reflux times needed for hydrolysis if both components of a dipeptide are hindered. These results suggest that microwave technology may be applicable to the digestion of biological samples [for recent examples, see Jassie, L. et al. [1994].

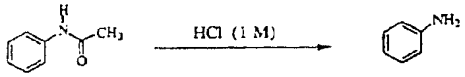
Williamson Ether Syntheses

The reaction of metal alkoxides with primary alkyl halides to form ethers is known as the Williamson ether synthesis and

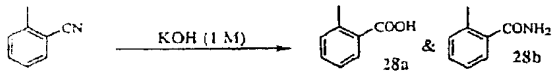
TABLE 8
Hydrolyses



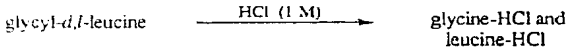
(26)	*Conventional*	*Microwave*
Solvent:	methanol - water	methanol - water
Reaction Temperature:	reflux (79°C)	130°→136°C (90 psi)
Yield:	60%	83%
Reaction Time:	36 hours	45 minutes



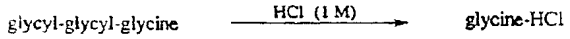
(27)	*Conventional*	*Microwave*
Solvent:	methanol - water	methanol - water
Reaction Temperature:	reflux (79°C)	141°→117°C (90 psi)
Yield:	98%	91%
Reaction Time:	4 hours	15 minutes



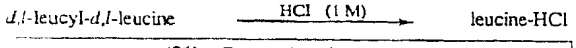
(28)	*Conventional*	*Microwave*
Solvent:	methanol - water	methanol - water
Reaction Temperature:	reflux (79°C)	130°C (90 psi)
Yield:	11% of **28a**; 70% of **28b**	5% of **28a**; 93% of **28b**
Reaction Time:	34 hours	15 minutes



(29)	*Conventional*	*Microwave*
Solvent:	water	water
Reaction Temperature:	reflux (100°C)	160°C (70 psi)
Yield:	73%	98%
Reaction Time:	12 hours	30 minutes



(30)	*Conventional*	*Microwave*
Solvent:	water	water
Reaction Temperature:	reflux (100°C)	156°C (90 psi)
Yield:	94%	98%
Reaction Time:	12 hours	15 minutes



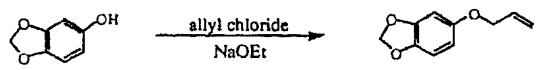
(31)	*Conventional*	*Microwave*
Solvent:	water	water
Reaction Temperature:	reflux (100°C)	158°C (70 psi)
Yield:	68%	89%
Reaction Time:	96 hours	3.5 hours

is recognized as the best way to make symmetrical and unsymmetrical ethers. Microwave heating proved superior to conventional heating in all cases studied (Table 9), most strikingly in the reaction of 2,6-dimethylphenol and allyl chloride. The steric effect of the methyl groups inhibits nucleophilic attack by the phenoxide on the allyl chloride, instead promoting deprotonation of ethanol (the solvent). The ethoxide anion generated *in situ* reacts with the allyl chloride present in the reaction mixture to account for the lower yields of the desired ether. Microwave heating improved the yield only modestly but greatly reduced the reaction time.

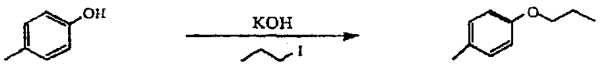
Aryl Methyl Ether Cleavage

Aryl methyl ethers can be readily cleaved by HBr using microwave heating (Table 10). The reaction proceeds by protonation of the ether oxygen followed by a nucleophilic attack on the methyl carbon by bromide. Electron-withdrawing

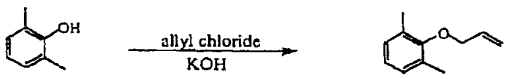
TABLE 9
Williamson Ether Syntheses.



(32)	*Conventional*	*Microwave*
Solvent:	ethanol	ethanol
Reaction Temperature:	reflux (78°C)	130°C (85 psi)
Yield:	89%	96%
Reaction Time:	60 minutes	1 minutes

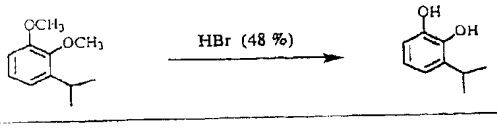


(33)	*Conventional*	*Microwave*
Solvent:	ethanol	ethanol
Reaction Temperature:	reflux (78°C)	131°C (90 psi)
Yield:	92%	96%
Reaction Time:	35 minutes	3 minutes

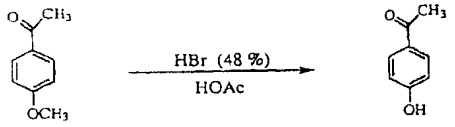


(34)	*Conventional*	*Microwave*
Solvent:	ethanol	ethanol
Reaction Temperature:	reflux (78°C)	131°C (90 psi)
Yield:	92%	96%
Reaction Time:	35 minutes	3 minutes

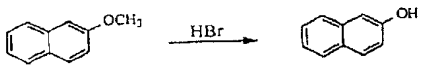
TABLE 10
Arl Ether Cleavage.



(35)	*Conventional*	*Microwave*
Solvent:	acetic acid	acetic acid
Reaction Temperature:	reflux (115°C)	152°→134°C (32 psi)
Yield:	97%	96%
Reaction Time:	3 hours	5 minutes



(36)	*Conventional*	*Microwave*
Solvent:	acetic acid	acetic acid
Reaction Temperature:	reflux (115°C)	170°→149°C (85 psi)
Yield:	47%	46%
Reaction Time:	52 hours	15 minutes



(27)	*Conventional*	*Microwave*
Solvent:	acetic acid	acetic acid
Reaction Temperature:	reflux (115°C)	156°→138°C (90 psi)
Yield:	81%	80%
Reaction Time:	72 hours	5 minutes

groups on the aryl ring decrease the basicity of the ether oxygen thereby retarding the reaction rate (cf. Entry 36).

The demethylation of β-naphthyl methyl ether (Entry 37) is very slow under conventional heating because the substrate is virtually insoluble in acetic acid. This is the second reaction (cf. Entry 24) for which the observed rate enhancement under microwave heating is most likely due to the increased solubility of the reactant at higher reaction temperatures.

Miscellaneous Reactions

This final section presents examples of other common reactions that can be carried out efficiently using microwave heating. The first three examples shown in Table 11 involve the base-promoted migration of a double bond into a more stable conjugated position; entries 39 and 40 also involve a subsequent tautomerization. While we were able to reproduce the published results for entries 38 [Chapman et al., 1971] and 39 [Davey and Hearne, 1964], in our hands the rearrangement of (E)-1-phenyl-2-buten-1-ol to butyrophenone (**40a**) failed [Iqbal and Jackson, 1968]. Instead, we obtained products which were derived from nucleophilic attack by anions of the solvent.

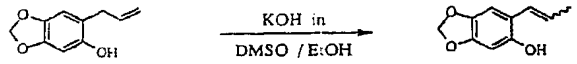
Several "Name Reactions" were also studied. The Beckmann rearrangement, the acid-catalyzed rearrangement of an oxime to an amide, is quite general in scope and clearly benefits from microwave heating (Entry 41). The condensation of the malonate derivative with urea in Entry 42 yields a barbituric acid derivative in high yield after only six minutes of heating. Most Friedel-Crafts alkylations are conducted at or below room temperature by using strong Lewis or protic acids but entry 43 is an exception which proceeds rapidly under mild acid conditions in a microwave oven. The Fischer indole synthesis, a powerful method for making indoles, involves the loss of ammonia from an arylhydrazone of an aldehyde or ketone when treated with an acid catalyst (cf. Entry 44). This reaction has been investigated by others using various conditions and microwave heating [Manhas et al, 1991; Abramovitch, 1992]. Finally, alkyl bromides react with magnesium to form Grignard reagents. However, in Example 45, formation of the Grignard reagent results in an elimination and ring opening.

Conclusions

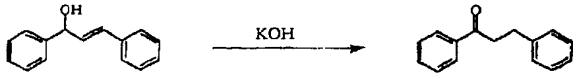
In organic chemistry a common rule of thumb is that the reaction rate for most reactions doubles for every ten degrees (°C) increase in the reaction temperature. This tenet is based on the Arrhenium equation. Since chemical kinetics are independent of the mode of heating and given the large sampling of reactions provided, an obvious equestion is: "How does the observed reaction rates using microwave heating compare to that observed using conventional methods ?" This data is summarized is Table 12. While no effort was made to optimize our microwave results, it is significant that thirty-three of the forty-five experiments carried out fall within simple Arrhenius expectations. We believe that further work would confirm that each of the twelve experiments which either exceed or occur at a rate less than that predicted would ultimately be found to conform with simple Arrhenius approximations.

The use of microwave heating in organic synthesis is still in its infancy. These transformations demonstrate that a large number of fundamental organic reactions occur more

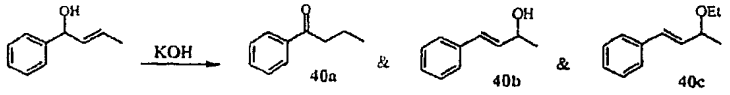
TABLE 11
Miscellaneous Reactions



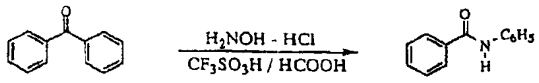
(38)	Conventional	Microwave
Solvent:	CMSO/ethanol	DMSO/ethanol
Reaction Temperature:	reflux (109°C)	170°C (41 psi)
Yield:	90%	80%
Reaction Time:	4 hours	3 minutes



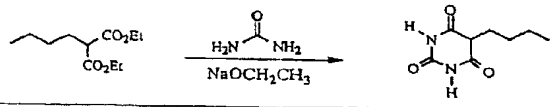
(39)	Conventional	Microwave
Solvent:	ethanol - water	ethanol - water
Reaction Temperature:	reflux (83°C)	145°C (90 psi)
Yield:	86%	97%
Reaction Time:	20 hours	10 minutes



(40)	Conventional	Microwave
Solvent:	ethanol/water	ethanol/water
Reaction Temperature:	reflux (83°C)	146°→144°C (90 psi)
Yield:	trace **40a**; 6% of **40b**; 2% of **40C**	2.4% of **40a**; 39% of **40b**; 16% of **40C**
Reaction Time:	4 days	10 minutes

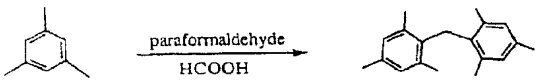


(41)	Conventional	Microwave
Solvent:	formic acid	formic acid
Reaction Temperature:	reflux (101°C)	171°C (90 psi)
Yield:	96%	99%
Reaction Time:	90 minutes	3 minutes

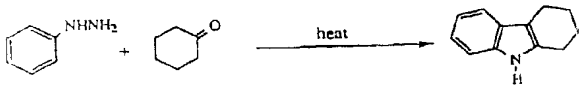


(42)	Conventional	Microwave
Solvent:	ethanol	ethanol
Reaction Temperature:	reflux (78°C)	142°C (90 psi)
Yield:	63%	80%
Reaction Time:	120 minutes	6 minutes

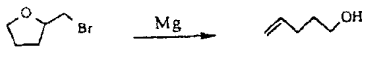
(Table 11 continued)



(43)	Conventional	Microwave
Solvent:	HCOOH	HCOOH
Reaction Temperature:	reflux (01°C)	130°→152°C (26 psi)
Yield:	72%	75%
Reaction Time:	90 minutes	4 minutes



(44)	Conventional	Microwave
Solvent:	CH_3COOH	CH_3COOH
Reaction Temperature:	reflux (118°C)	118°C (46 psi)
Yield:	100%	100%
Reaction Time:	15 minutes	2 minutes



(45)	Conventional	Microwave
Solvent:	diethyl ether	diethyl ether
Reaction Temperature:	reflux (36°C)	106°→105°C (90 psi)
Yield:	44%	38%
Reaction Time:	3 hours	10 minutes

rapidly and in comparable yield using microwave heating rather than conventional heating procedures. Not surprisingly, we expect this area to continue to be the focus of extensive activity.

Experimental Section

General Procedures

All solvents were distilled prior to use. Ether implies diethyl ether except when otherwise specified.

Standard ethereal workup consisted of partitioning the reaction mixture between ether and water, and then drying the organic phase with a saturated brine wash and then over anhydrous magnesium sulfate. The resulting solution was concentrated to a residue at water aspirator pressure. Chromatography was performed on silica gel. In each control experiment the workup, isolation, and analytical procedures used in the original were duplicated.

Acid-washed activated MnO_2 used in the oxidation studies was prepared by the method of Harfenist et al. [1954]. The diene used in Entry 12 was prepared by the Birch reduction of *o*-xylene. The propargylic alcohol used in Entry 9 was prepared by acetylenide addition to 6-methyl-5-hepten-2-one. The diene used in Entry 5 was obtained by treating cyclohexanone with vinyl magnesium bromide and subsequently dehydrating the resulting alcohol with phosphoric acid. The diol used in Entry 22 was obtained by lithium aluminum hydride reduction of Weland-Miescher ketone, prepared by the procedure of Ramachandran and Newman [1973]. Preparations for the alcohols used in Entries 36 and 37 are found in the literature [Davey and Hearne, 1964, respectively]. The tetrahydrofurfuryl bromide used in Entry 44 was prepared from the corresponding alcohol by treatment with PBr_3. Other compounds were obtained from commercial sources.

Where compositions of mixtures are given from ^1H NMR analysis, spectra were taken at 250 or 300 MHz and the molar ratios of the components were determined by integrating convenient, fully resolved signals and converting to the appropriate mass percent; where mass and net yield figures follow, these were calculated from the mass percent.

The following abbreviations are used: DMF for dimethylformamide, DMSO for dimethylsulfoxide, THF for tetrahydrofuran, and psi for pounds per square inch gauge.

Example (1). 1,4-Diphenyl-1,3-butadiene (1.00 g, 4.85 mmol) and diethyl acetylenedicarboxylate (1.23 g, 7.23 mmol) in DMF (15 mL) were heated at 70% power to 30 psi. This pressure was maintained for twenty minutes during which time the reaction temperature declined from 198°C to 194°C. The reaction mixture was then cooled to 0°C. After standard ethereal workup, the crude residue was chromatographed (hexanes-ether, 20:1, followed by 10:1) to isolate the adduct as a pale yellow solid (1.05 g, 58%).

In a control experiment, an identical reaction mixture required six hours of reflux (oil bath) for completion. Identical workup and chromatography gave 1.22 g (67%) of the adduct.

Example (2). Furan (2.00 g, 29.41 mmol) and diethyl acetylenedicarboxylate (1.00 g, 5.88 mmol) in DMF (15 mL) were heated at 80% power to 30 psi. This pressure was maintained for ten minutes during which time the reaction temperature declined from 163°C to 147°C. The reaction mixture was then cooled to 0°C. After standard ethereal workup, the crude residue was chromatographed (hexanes-ether, 10:1) to give an amber colored oil (1.20 g, 86%).

The control experiment was performed on a reduced scale (diethyl acetylenedicarboxylate: 143 mg, 0.84 mmol; furan: 286 mg, 4.20 mmol; DMF: 2 mL) in a sealed tube. The reaction vessel was placed in a preheated oil bath maintained for

TABLE 12

Example	Conventional Time (minutes)	Microwave Time (minutes)	Initial Ratio	Arrhenius Factor	Corrected Ratios	
1	360	20	18	19.7	0.91	N
2	15	10	1.5	0.25	6.00	P
3	45	4	11.3	13	0.87	N
4	120	12	10	18.4	0.54	N
5	60	30	2	19.7	0.10	M
6	4800	300	40	18.4	2.17	N
7	2160	5	432	18.4	23.48	P
8	5760	20	288	18.4	15.65	P
9	5760	480	12	21.1	0.57	N
10	20	1	20	24.2	0.83	N
11	2400	20	120	7.5	16.00	P
12	300	20	15	7.2	2.08	N
13	300	20	15	6.5	2.31	N
14	30	10	3	4	0.75	N
15	20	0.5	40	16	2.50	N
16	30	0.5	60	15	4.00	N
17	40	4	10	7	1.43	N
18	30	10	3	7	0.43	N
19	4800	240	20	32	0.63	N
20	480	7	69	111	0.62	N
21	300	3	100	256	0.39	N
22	90	7	12.9	104	0.12	M
23	80	1	80	45	1.78	N
24	2520	30	84	27	3.11	N
25	90	2	45	119	0.38	N
26	2160	45	48	42	1.14	N
27	240	15	16	32	0.50	N
28	2040	15	136	34	4.00	N
29	720	30	24	64	0.38	N
30	720	15	48	49	0.98	N
31	5760	210	27	60	0.45	N
32	60	1	60	37	1.62	N
33	35	3	12	40	0.30	N
34	210	4	52	28	1.86	N
35	180	5	36	7	5.14	P
36	3120	15	2108	22	9.45	P
37	4320	5	864	12	72.00	P
38	240	3	80	69	1.16	N
39	1200	10	120	73.5	1.63	N
40	5760	10	576	73.5	7.84	P
41	90	3	30	128	0.23	N
42	120	6	20	42.2	0.47	N
43	90	4	22.5	10.5	2.14	N
44	15	2	7.5	52	0.14	M
45	180	10	18	119	0.15	M

at 175 °C for fifteen minutes. Identical workup and chromatography gave 135 mg (68%) of the adduct.

Example (3). Anthracene (2.00 g, 11.20 mmol) and maleic anhydride (1.00 g, 10.20 mmol) in DMF (25 mL) were heated at 70% power to 15 psi. The temperature remained constant at 190°C while this pressure was maintained for four minutes. The reaction mixture was then cooled to 0°C. After standard ethereal workup, the crude residue was recrystallized from xylenes to give colorless needles (2.60 g, 84%).

As the control, an identical reaction mixture was refluxed for forty-five minutes (oil bath). Identical workup and purification gave 2.65 g (86%).

Example (4). Anthracene (1.85 g, 10.38 mmol) and dimethyl fumarate (1.00 g, 6.94 mmol) in DMF (15 mL) were heated at 80% power to 20 psi. This pressure was maintained for twelve minutes during which time the temperature declined from 197 °C to 192 °C. The vessel was cooled, the contents were diluted with brine and then extracted twice with a mixture of THF and ether (1:1). The combined organic phases were washed with water, dried over anhydrous magnesium sulfate and concentrated at reduced pressure. Unreacted diethyl fumarate was removed from the residue by heating two hours at 60°C and 0.5 mm pressure. The Diels-Alder adduct, which proved inseparable chromatographically from unreacted anthracene, was saponified by refluxing overnight with 2 g of KOH in THF (10 mL) and water (5 mL). This mixture was diluted with ether, then extracted with 5% aqueous NaOH. The combined aqueous phases were washed with ether, then acidified to pH < 2 with concentrated HCl, and extracted with ether. The organic phase was washed with water, dried over anhydrous magnesium sulfate, and concentrated. Residual THF was removed by heating for six hours at 75 °C at 1 mm. The diacid remained as a white solid (1.54 g, 75%).

As the control, an identical reaction mixture was refluxed for two hours (oil bath). The diacid (1.67 g, 82%) was obtained by the same workup, saponification, and isolation procedures.

Example (5). 1-Vinylcyclohexene (1.00 g, 9.26 mmol) and diethyl oxomalonate (0.80 g, 4.63 mmol) in DMF (15 mL) were heated at 70% power to 23 psi. This pressure was maintained for thirty minutes during which time the reaction temperature declined from 198 °C to 192 °C. The reaction mixture was then cooled to 0 °C. After standard ethereal workup the crude residue was chromatographed (hexanes-ether, 10:1) to isolate the adduct (744 mg, 57%) as a colorless oil.

As the control, an identical mixture was refluxed using an oil bath for a one-hour period. The same workup and isolation procedures gave 713 mg (55%) of adduct.

Example (6). Allyl phenyl ether (1.00 g, 7.45 mmol) in DMF (15 mL) was heated at 70% power to 30 psi. This pressure was maintained for five hours during which time the reaction temperature declined from 198°C to 193°C. The reaction mixture was then cooled to 0°C. After standard ethereal workup, the residue was chromatographed (hexanes-ether, 20:1 followed by 3:1) to give *o*-allylphenol (800 mg, 80%).

As the control, an identical reaction mixture was refluxed for eighty hours (oil bath). The same workup and isolation procedures gave 230 mg (23%) of the rearrangement product.

Example (7). Sesamol allyl ether (5.12 g, 28.82 mmol) in DMF (10 mL) was heated at 50% power to 30 psi. This pressure was maintained for five minutes during which time the reaction temperature remained at 195°C. After cooling, the mixture was diluted with water and extracted with ether. The organic phase was extracted with 5% NaOH, and the resulting aqueous solution was acidified to pH < 2 by addition of concentrated HCl and extracted with ether. This ethereal solution was dried over anhydrous magnesium sulfate and concentrated to give allylsesamol (4.96 g, 97%) as an amber-colored oil.

As the control, an identical mixture was refluxed for thirty-six hours (oil bath). Identical isolation procedures gave 2.08 g (72%) of allylsesamol.

Example (8). Allyl 2,6-dimethylphenyl ether (2.00 g, 12.30 mmol) in DMF (15 mL) was heated at 70% power to 17 psi. This pressure was maintained for twenty minutes during which time the reaction temperature declined from 197°C to 192°C. The reaction mixture was then cooled to 0°C. After standard ethereal workup, the crude residue was chromatographed (hexanes followed by hexanes-ether 10:1) to obtain the rearrangement product (1.81 g, 91%) as a colorless oil.

As a control experiment, an identical mixture was refluxed for four days (oil bath). Identical isolation gave 1.65 g (83%) of adduct.

Example (9). 3,7-Dimethyl-6-octen-1-yn-3-ol (1.00 g, 6.57 mmol) in DMF (15 mL) was heated at 70% power to 23 psi. This pressure was maintained for eight hours during which time the reaction temperature declined from 198°C to 196°C. The reaction mixture was then cooled to 0°C. After standard ethereal workup, the crude residue was chromatographed. The diastereomeric cyclopentanols [328 mg (33%) and 115 mg (40%) in order of elution] were isolated as colorless oils by chromatography (hexanes-ether, 40:1 gradient to 4:1). Relative configurations were not assigned.

As the control, an identical reaction mixture was refluxed for four days using an oil bath, although TLC analysis indicated the reaction was not complete. The same products [151 mg (15%) and 181 mg (18%) in order of elution] were isolated by the same procedures.

Example (10). β-Pinene (1.00 g, 7.34 mmol) and diethyl ketomalonate (2.55 g, 14.68 mmol) in DMF (15 mL) were heated at 70% power to 20 psi. This pressure was maintained for one minute during which time the reaction temperature remained at 199°C. The reaction mixture was then cooled to 0°C and standard ethereal workup gave 1.83 g of a crude residue. Chromatography (hexanes followed by hexanes-ether, 10:1) provided 1.62 g of adduct (71%) as a colorless oil.

As the control, an identical mixture was refluxed for twenty minutes (oil bath). Identical workup and isolation gave 1.55 g (68%) of adduct.

Example (11). Diethyl acetylenedicarboxylate (0.50 g, 3.52 mmol), 1,4-cyclohexadiene (4.23 g, 52.82 mmol) and DMF (5 mL) were heated at 100% power to 90 psi. This pressure was maintained for twenty minutes during which time the reaction temperature declined from 184°C to 179°C. The reaction mixture was then cooled to 0°C. After standard ethereal workup, solvent removal and recovery of excess 1,4-cyclohexadiene were accomplished by means of fractional distillation. The remaining residue was chromatographed (hexanes-ether, 20:1 followed by 10:1) to give the tricyclic product (386 mg, 49%) as a colorless oil.

As the control, an identical reaction mixture was refluxed for forty hours using an oil bath, however, TLC analysis indicated that the reaction was not complete. Identical workup and isolation procedures gave 108 mg (14%) of tricyclic product.

Example (12). Diethyl acetylenedicarboxylate (0.50 g, 3.52 mmol), 1,2-dimethyl-1,4-cyclohexadiene (5.71 g, 52.82 mmol) and 5 mL of DMF were heated at 100% power to 30 psi. This pressure was maintained for twenty minutes during which time the reaction temperature declined from 183°C to 180°C. The reaction mixture was then cooled to 0°C. After standard ethereal workup, the excess diene was recovered as described in Example 11. The remaining residue was chromatographed (hexanes-ether, 20:1 followed by 10:1) to isolate 12a (690 mg, 78%) as a colorless oil. Fractions containing 12b plus an impurity inseparable in the hexanes-ether system were rechromatographed (hexanes-ethyl acetate, 10:1) to isolate 150 mg (17%) of 12b as a colorless oil.

As the control, an identical mixture was refluxed for five hours (oil bath). Adducts 12a (240 mg, 24%) and 12b (50 mg, 5%) were isolated by means of the same isolation procedures.

Example (13). Diethyl acetylenedicarboxylate (0.50 g, 3.52 mmol), bicyclo[4.3.0]nona-3,6(1)-diene (7.47 g of commercially available 85%, 53.00 mmol) and DMF (5 mL) were heated at 100% power to 15 psi. This pressure was maintained for twenty minutes during which time the reaction temperature declined from 182°C to 178°C. The reaction mixture was then cooled to 0°C. After standard ethereal workup, the crude residue was chromatographed (hexanes-ether, 20:1 followed by 10:1 then 5:1) to isolate the tetracyclic adduct as a colorless oil (634 mg, 69%). The excess diene was recovered from the early fractions.

As the control, an identical reaction mixture was refluxed for five hours (oil bath). Identical workup and purification gave 380 mg (41%) of the adduct.

Example (14). Cyclohexanol (2.00 g, 20.00 mmol) was added to a solution of NaBr (3.10 g, 30.12 mmol) in 7 mL of concentrated H_2SO_4 and 7 mL of water. The mixture was heated at 70% power to 10 psi. This pressure was maintained for ten minutes during which time the reaction temperature rose from 137°C to 140°C. After cooling, the mixture was diluted with water and extracted with hexanes. The organic phase was washed with brine containing a trace of $NaHSO_3$ and dried over anhydrous $MgSO_4$. Removal of the volatiles under reduced pressure gave cyclohexyl bromide (1.60 g, 49%) as an amber-colored oil.

As the control an identical mixture was refluxed for thirty minutes (oil bath). Identical isolation procedures gave 1.09 g (33%).

Example (15). 1,8-Octanediol (1.00 g, 6.85 mmol) was added to a solution of NaBr (2.12 g, 20.61 mmol) in 7 mL of concentrated H_2SO_4 and 7 mL of water. The mixture was heated at 70% power to 15 psi. This pressure was maintained for thirty seconds during which time the reaction temperature remained at 158°C. The dibromide (1.12 g, 60%) was isolated as described in example 14.

As the control, an identical mixture was refluxed for twenty minutes (oil bath). Identical workup gave 1.30 g of dibromide (70%).

Example (16). 1,10-Decanediol (1.00 g, 5.74 mmol) was added to a solution of NaBr (1.48 g, 14.3 mmol) in 7 mL of concentrated H_2SO_4 and 7 mL of water. The mixture was heated at 100% power to 15 psi. This pressure was maintained for thirty seconds during which time the reaction temperature increased from 156°C to 158°C. The reaction mixture was then cooled to 0°C. After standard ethereal workup,

the crude residue was chromatographed (hexanes followed by hexanes-ether 1:1) to isolate bromide 16a (643 mg, 37%) and dibromide 16b (406 mg, 24%) as colorless oils.

As a control experiment, an identical mixture was refluxed for thirty minutes using an oil bath and subjected to identical workup and separation techniques to give 310 mg (23%) of 16a and 57 mg (3%) of 16b.

Example (17). 1-Bromohexane (2.35 g, 14.22 mmol) was added to a solution of NaI (3.20 g, 21.4 mmol) in 2-butanone (20 mL). The mixture was heated at 70% power to 20 psi and 108°C. These conditions were maintained for four minutes. After cooling, the mixture was diluted with water and extracted with ether. The organic phase was washed with water containing a trace of $NaHSO_3$ and dried over anhydrous magnesium sulfate. The solvent was removed at reduced pressure to leave the iodide (2.51 g, 83%) along with a trace (< 1% by ^1H NMR analysis) of unreacted 1-bromohexane.

As the control, an identical mixture was refluxed (oil bath) while monitored by GC analysis. Conversion was 99% complete after forty minutes. Identical workup gave 2.45 g (81%) containing < 1% of unreacted bromide (^1H NMR analysis).

Example (18). 1-Bromooctane (2.24 g, 11.60 mmol) was added to a solution of NaI (2.60 g, 17.40 mmol) in 20 mL of 2-butanone. The mixture was heated at 70% power to 20 psi and 108 °C for a ten-minute period. After cooling, the mixture was diluted with water and extracted with ether. The organic phase was washed with brine containing a trace of $NaHSO_3$ and dried over anhydrous magnesium sulfate. The solvent was removed at reduced pressure to leave the iodide (2.50g, 90%).

As the control, an identical reaction mixture was refluxed (oil bath) while monitored by GC analysis. Conversion was 99% complete after thirty minutes. Identical workup gave 2.17 g of iodide (78%).

Example (19). Cyclohexyl bromide (2.65 g, 16.33 mmol) was added to a solution of NaI (3.65 g, 24.44 mmol) in 20 mL of 2-butanone. The mixture was heated at 70% power to 20 psi. This pressure was maintained for four hours during which time the temperature decreased from 131°C to 129°C. The reaction mixture was then cooled to 0°C. The workup used in Example 18 gave 3.02 g of cyclohexyl iodide (72% net yield) of 85% purity (^1H NMR analysis).

As a control, an identical mixture was refluxed (oil bath) while monitored by GC analysis. After eighty hours significant cyclohexyl bromide was still present. Identical workup gave 3.00 g (72% net yield) of 85% purity (^1H NMR analysis).

Example (20). Benzyl alcohol (0.50 g, 4.60 mmol) and activated MnO_2 (2.00 g, 23.00 mmol) were placed in a quartz vessel (cf. Figure 1). After purging with dry nitrogen, anhydrous ether (10 mL) was introduced by syringe. The mixture was heated at 20% power to 90 psi and 104°C. These conditions were maintained for seven minutes. After cooling, the oxidant was removed by filtration through Celite and the solvent was removed at reduced pressure. Pure benzaldehyde (254 mg, 52%) and unreacted starting material were isolated by chromatography (hexanes-ether, 10:1).

As a control experiment, an identical mixture was refluxed for eight hours using an oil bath and separated to give 102 mg (20%) of benzaldehyde and the balance of the starting material.

Example (21). *trans*-Cinnamyl alcohol (0.50 g, 3.70 mmol) and activated MnO_2 (2.00 g, 23.00 mmol) were placed in a quartz reaction vessel (cf. Figure 1). After purging with nitrogen, anhydrous ether (10 mL) was introduced by syringe. The mixture was heated at 20% power to 90 psi and 116°C. These conditions were maintained for three minutes. The reaction mixture was then cooled to 0°C. The oxidant was removed by filtration through Celite and the solvent was removed at reduced pressure. *trans*-Cinnamaldehyde (402 mg, 82%) and the balance of the starting material were separated by column chromatography (hexanes-ether, 10:1).

As the control, an identical mixture was refluxed for five hours (oil bath) and separated to give 219 mg (44%) of the aldehyde and the balance of the starting material.

Example (22). 1,2,3,4,6,7,8,8a-Octahydro-8a-methyl-1,6-naphthalenediol (200 mg, 1.10 mmol) and activated MnO_2 (2.00 g, 23.00 mmoL) were placed in a quartz reaction vessel (Figure 1). After purging with dry nitrogen, anhydrous ether (10 mL) was introduced by syringe. The mixture was heated at 20% power to 90 psi. This pressure was maintained for seven minutes during which time the temperature was constant at 103°C. The enone product (157 mg, 79%) and the balance of the starting material were separated by column chromatography (hexanes-ether, 4:1 followed by 1:1).

As the control, an identical reaction mixture was refluxed for ninety minutes (oil bath) and separated as above to give 66 mg (33%) of the product and the balance of the starting material.

Example (23). Benzoic acid (6.1 g, 49.18 mmol) was added to a mixture of concentrated H_2SO_4 (2 mL) and 25 mL of methanol. The reaction mixture was heated at 20% power to 50 psi for one minute during which time the reaction temperature was maintained at 120°C. Standard ethereal workup gave 6.23 g of methyl benzoate (92%).

As the control, an identical mixture was refluxed for eighty minutes using an oil bath and worked up to give 6.24 g (92%) of the ester.

Example (24). 2,2'-Bis(cyclohexanecarboxylic acid) (500 mg, 19.72 mmol) was added as a powder to a mixture of concentrated H_2SO_4 (0.5 mL) and methanol (5 mL). The diacid proved almost totally insoluble in this mixture. The mixture was heated at 35% power to 70 psi for thirty minutes during which time the reaction temperature declined from 118°C to 108°C. Standard ethereal workup gave the diester (470 mg, 85%) as a white crystalline solid.

In a control experiment, an identical mixture was refluxed for forty-two hours using an oil bath. Identical workup gave 537 mg (97%) of the diester.

Example (25). 2-Methyl-1,3-cyclopentandione (2.00 g, 18.23 mmol) was added to a solution of *p*-toluenesulfonic acid (100 mg, 0.53 mmol) in 15 mL of methanol. The mixture was heated at 70% power to 90 psi for two minutes during which time the reaction temperature rose from 132°C to 136°C. The mixture was cooled with brine and extracted with methylene chloride (4 x 50 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$, dried over anhydrous magnesium sulfate and concentrated. The residue was chromatographed (methylene chloride-methanol, 10:1) to isolate the vinylogous ester (1.93 g, 86%).

As the control, an identical mixture was refluxed for ninety minutes (oil bath). Identical workup and isolation procedures gave 1.89 g (84%) of the cyclopentenone.

Example (26). Acetanilide (1.00 g, 7.41 mmol) was added to a 1 N solution (20 mL) of KOH in methanol-water (1:1). The mixture was heated at 35% power to 90 psi. This pressure was maintained for forty-five minutes during which time the reaction temperature increased from 130°C to 136°C. Standard ethereal workup, followed by chromatography, gave 571 mg of aniline (83%).

As the control, an identical mixture was refluxed thirty-six hours using an oil bath and worked up to give 413 mg (60%) of aniline.

Example (27). Acetanilide (1.00 g, 7.41 mmol) was added to a 1 N solution of HCl (20 mL) in methanol-water (1:1). The mixture was heated at 35% power to 90 psi. This pressure was maintained for 15 minutes during which time the reaction temperature declined from 141°C to 117°C. The cooled mixture was neutralized with saturated aqueous $NaHCO_3$. Standard ethereal workup, followed by chromatography, gave 628 mg (91%) aniline.

As the control, an identical mixture was refluxed for four hours (oil bath) and worked up to give 679 mg (98%) of aniline.

Example (28). *o*-Toluonitrile (1.00 g, 8.55 mmol) was added to a 1 N solution (20 mL) of KOH in methanol-water (1:1). The mixture was heated at 35% power to 90 psi. This pressure was maintained for fifteen minutes during which time the reaction temperature remained at 130°C. The cooled mixture was diluted with saturated brine, acidified (pH < 2 by the addition of concentrated HCl) and extracted with methylene chloride (3 x 30 mL). The combined organic extracts were dried over anhydrous mangesium sulfate and concentrated to give a white solid (1.13 g) consisting of *o*-toluamide (95% by ^{1}H NMR analysis, 107 mg, 93% net yield) and *o*-toluic acid (5% by ^{1}H NMR analysis, 57 mg, 5% net yield).

An identical reaction mixture was refluxed for thirty-four hours using an oil bath and gave a mixture (935 mg) of the amide (86% by ^{1}H NMR analysis, 804 mg, 70% net yield) and the acid (14% by ^{1}H NMR analysis, 131 mg, 11% net yield.)

Example (29). Glycyl-*d,l*-leucine (200 mg, 1.06 mmol) was dissolved in 1 N aqueous HCl (10 mL). The solution was heated at 70% power to 70 psi. This pressure was maintained for thirty minutes during which time the reaction temperature was constant at 160°C. The mixture was lyophilized to constant weight (290 mg, 98%) at < 1mm pressure.

As the control, an identical mixture was refluxed for twelve hours (oil bath). Using the same workup procedure gave 216 mg (73%) of amino acid salts.

Example (30). Glycylglycylglycine (200 mg, 1.06 mmol) was dissolved in 1 N aqueous HCl (10 mL). The solution was heated at 70% power to 90 psi. This pressure was maintained for fifteen minutes during which time the reaction temperature remained at 156°C. The mixture was lyophilized to constant weight (348 mg, 98%) at < 1mm pressure.

As the control, an identical solution was refluxed for twelve hours using an oil bath. The use of conventional heating gave 331 mg (94%) of hydrochloride salts.

Example (31). *d,l*-Leucyl-*d,l*-leucine (200 mg, 0.82 mmol) was dissolved in 1 N aqueous HCl (10 mL). The solution was heated at 70% power to 70 psi. This pressure was maintained for 3 and a half hours during which time the reaction temperature increased from 158°C to 160°C. The mixture was lyophilized to constant weight (243 mg, 89%) at < 1mm.

As the control, an identical mixture was refluxed for ninety-six hours (oil bath). The same workup procedure as described above yielded 185 mg (68%) of leucine hydrochloride salt.

Example (32). Sodium (0.49 g, 21.30 mmol) was dissolved in 13 mL of absolute ethanol under nitrogen. The solution was transferred to the microwave vessel which was then sealed. A solution of sesamol (2.50 g, 18.00 mmol) in absolute ethanol (5 mL) followed by allyl chloride (2.10 g, 27.03 mmol) was added by syringe through one of the tubing fittings. The mixture was heated at 35% power to 85 psi. This pressure was maintained for one minute during which time the reaction temperature remained at 130°C. The cooled mixture was diluted with water and extracted with ether. The combined organics were washed with 5% aqueous NaOH, water, dried over anhydrous magnesium sulfate and concentrated to give the ether (3.11 g, 96%) as a light brown oil.

As the control, an identical mixture was refluxed for one hour (oil bath). Identical isolation procedures gave 2.88 g (89%) of the desired ether.

Example (33). *p*-Cresol (2.22 g, 20.55 mmol) and propyl iodide were added to alcoholic KOH (15 mL, 10% w/v) and the mixture was heated at 70% power to 90 psi. This pressure was maintained for three minutes during which time the reaction temperature was constant at 131 °C. After standard ethereal workup, the crude residue was chromatographed (hexanes-ether, 10:1) to give the ether (2.96 g, 96%) as a colorless oil.

As the control, an identical mixture was refluxed for thirty-five minutes using an oil bath. Identical workup and purification gave 2.84 g (92%) of the desired ether.

Example (34). 2,6-Dimethylphenol (5.00 g, 40.98 mmol) and allyl chloride (4.69 g, 61.47 mmol) were added to a solution of KOH (2.75 g, 49.16 mmol) in 20 mL of methanol. The mixture was heated at 70% power to 90 psi. This pressure was maintained for four minutes during which time the reaction temperature was constant at 126°C. The cooled mixture, which was not basic and contained some unreacted phenol, was worked up using ether and chromatographed (elution with hexanes) to provide the ether (4.60 g, 69%) as a colorless oil.

As the control, an identical mixture was refluxed for three and one half hours (oil bath). Identical workup and chromatography gave 4.17 g (63%) of the ether.

Example (35). 3-Isopropylveratrole (500 mg, 2.77 mmol) was added to a mixture of 10 mL of aqueous (48%) HBr and 10 mL of acetic acid. The mixture was heated at 100% power to 32 psi for five minutes during which time the reaction temperature declined from 152°C to 134°C. Following standard ethereal workup, the crude residue was chromatographed (hexanes-ether, 10:1) and provided 407 mg of the catechol (96%).

As the control, an identical mixture was refluxed for three hours (oil bath). Identical isolation gave 409 mg (97%) of catechol.

Example (36). *p*-Methoxyacetophenone (2.00 g, 13.33 mmol) was added to a mixture of 10 mL of aqueous (48%) HBr and 10 mL of acetic acid. The mixture was heated at 100% power to 85 psi and maintained for fifteen minutes during which time the reaction temperature declined from 170°C to 149°C. After standard ethereal workup the residue was chromatographed (hexanes-ether, 5:1 gradient to 1:1) to give the phenol (840 mg, 46%).

As the control, an identical mixture was refluxed for fifty-two hours (oil bath). Identical isolation gave 869 mg (47%).

Example (37). β-Naphthyl methyl ether (2.00 g, 12.64 mmol) was added to a mixture of 10 mL of aqueous (48%) HBr and 10 mL of acetic acid. The mixture was heated at 100% power to 90 psi and maintained for five minutes, during which time the reaction temperature declined from 156°C to 138°C. After standard ethereal workup the residue was chromatographed (hexanes-ether, 5:2) to give 1.45 g of β–naphthol (80%).

As the control, an identical mixture was refluxed for seventy-two hours (oil bath). Identical isolation gave 1.47 g (81%) of β-naphthol.

Example (38). 2-Allyl sesamol (200 mg, 1.12 mmol) in DMSO (10 mL) was added to a solution of KOH (500 mg, 8.90 mmol) in 5 mL of ethanol. The mixture was heated at 35% power to 41 psi for three minutes during which time the reaction temperature remained at 170°C. The cooled mixture was acidified (pH < 2) by the addition of concentrated HCl and extracted with ether. Standard ethereal workup gave 178 mg of crude residue which was purified by chromatography (hexanes-ether, 1:1) to give the isomerized product (160 mg, 80%) as light-brown crystals.

An identical mixture was refluxed for four hours using conventional heating (oil bath) and subjected to identical workup and chromatography to give 179 mg (90%) of the same product. In both cases a negligible trace of unreacted starting material remained which proved chromatographically inseparable from the product.

Example (39). Chalcol (1.00 g, 4.76 mmol) was added to a solution (25 mL) of KOH (20%, w/v) in aqueous ethanol (60%, v/v). The mixture was heated at 100% power to 90 psi for ten minutes during which time the reaction temperature remained at 145°C. The cooled mixture was acidified (pH < 2) by the addition of concentrated HCl. Standard ethereal workup gave 965 mg (97%) of the rearrangement product as pale yellow crystals.

As the control, an identical mixture was refluxed for twenty hours (oil bath). Identical workup gave 861 mg (86%).

Example (40). 1-Phenyl-2-buten-1-ol (1.00 g, 6.75 mmol) was added to a solution of KOH (5.0 g) in an ethanol-water mixture (3:2, 25 mL). The mixture was heated at 100% power to 90 psi for ten minutes during which time the reaction temperature declined from 146°C to 144°C. After standard ethereal workup, the residue was chromatographed (hexanes-ether, 20:1 gradient to 1:1). The early fractions gave a mixture (215 mg) of 40a (11% of mass by 1H NMR , 24 mg, 2.4% net yield) and 40c (89% of mass by ^{1}H NMR, 191 mg, 16% net yield). From later fractions were obtained unreacted starting material (210 mg, 21%) and 40b (388 mg, 39%). All were colorless oils.

As the control, an identical reaction mixture was refluxed using an oil bath. After four days the mixture still contained predominantly starting material (TLC analysis). After workup the residue was subjected to ^{1}H NMR analysis. The crude oil (915 mg) contained 40b (7% of mass, 64 mg, 6% net yield), 40c (3% of mass, 27 mg, 2% net yield) and a negligible trace of 40a, with the balance unreacted starting material.

Example (41). Benzophenone (1.00 g, 5.50 mmol) and hydroxylamine hydrochloride (510 mg, 7.30 mmol) were added to a solution of triflic acid (2 drops) in 90% formic acid (5 mL). The mixture was heated at 35% power to 90 psi and was maintained for three minutes during which time the reaction temperature remained at 171°C. The cooled mixture was diluted with water and extracted with methylene chloride (3 x 30 mL). The organic phase was dried over anhydrous magnesium sulfate and concentrated. The residue was recrystallized (95% ethanol, 5% water) to give colorless crystals (1.07 g, 99%).

As the control, an identical mixture was refluxed for ninety minutes using an oil bath. Identical workup and recrystallization gave 1.04 g (96%).

Example (42). Sodium (460 mg, 20.00 mmol) was dissolved in absolute ethanol (20 mL) under nitrogen. This solution was transferred to a Teflon microwave vessel and *n*-butyldiethymalonate (4.32 g, 20.00 mmol) was added followed by urea (1.20 g, 20.00 mmol) dissolved in 22 mL of ethanol. The mixture was heated at 35% power to 90 psi. This pressure was maintained for six minutes during which time the reaction temperature was constant at 142°C. The cooled mixture was acidified to pH < 2 by the addition of concentrated HCl, concentrated to approximately 50% of the original volume and chilled in ice. The crystalline condensation product (293 mg, 80%) was filtered and washed with cold water.

An identical reaction mixture was refluxed for two hours using an oil bath after which a trace of starting material remained. Identical crystallization gave 2.31 g (63%) for this control experiment.

Example (43). Mesitylene (3.15 g, 26.20 mmol) and paraformaldehyde (375 mg which is equivalent to 12.50 mmol formaldehyde) were added to 90% formic acid (2.3 mL). The mixture was heated at 35% power to 26 psi. The temperature increased from 130°C to 142°C during a four-minute period. The mixture was permitted to cool to room temperature, then chilled in ice, and crystallization was initiated by seeding. The crystals (2.34 g, 75%) were washed with aqueous $NaHCO_3$ and then cold hexanes.

As the control, an identical mixture was refluxed for ninety minutes using an oil bath. Crystallization began spontaneously upon cooling to room temperature . The crystalline product (2.27 g, 72%) was filtered and washed as above.

Example (44). Freshly distilled phenylhydrazine (4.55 g, 4.21 mmol), cyclohexanone (5.21 g, 53.10 mmol) and glacial acetic acid (40 mL) were heated at 35% power to 46 psi and 175°C. These conditions were maintained for two minutes. The mixture was cooled, diluted with water and the resulting precipitate was filtered and washed with 75% ethanol. The tan powder (7.21g, 100%) was nearly pure by ^{1}H NMR analysis.

As the control, an identical mixture was refluxed for fifteen minutes (oil bath). Identical workup gave 7.19 g (100%).

Example (45). Magnesium turnings (479 mg, 19.70 mmol) and 25 mg of iodine were placed in a quartz vessel (Figure 1). The reaction vessel was capped and purged with dry nitrogen through one of the tubing fittings. Tetrahydrofurfuryl bromide (650 mg, 3.94 mmol) in 10 mL of anhydrous ether was added by syringe through the tubing fitting. The mixture was heated at 35% power to 90 psi for ten minutes during which time the reaction temperature dropped from 106° to 105°C. The cooled mixture was quenched with saturated aqueous NH_4Cl (1 mL) and benzene (20 µL) was added as an internal standard for GC analysis. The mixture contained 0.15 mmol / mL (38% yield) of the alcohol by GC analysis.

As the control experiment an identical mixture was refluxed for three hours using an oil bath. Identical quenching and analytical procedures indicated 0.17 mmol / mL (44% yield).

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